DE GRUYTER Pure Appl. Chem. 2025; 97(4): 279–330

Review

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Blockchain technology: driving change in the scientific research workflow

https://doi.org/10.1515/pac-2023-1204

Abstract: The goal of this white paper is to present an objective overview of the current use of blockchain technology along the scientific research workflow and in related areas such as chemical/drug supply chains and education. It represents the culmination of three years of data gathering, including input from multiple interviews with pioneer users of the technology, as well as from more recent adopters around the globe, and recent industry technology analysts' reports. Within these pages are descriptions of successful applications of the technology at each step of the scientific research workflow – from the timestamping of ideas to funding, to actual experimentation, to the analysis of research results, and ultimately to the sharing of information and the publication of results. However, not all blockchain use cases have such a successful conclusion. In this white paper you will learn where the technology has not worked – and why – thanks to those interviewed who discussed in detail the lessons that they themselves learned during their own blockchain journey. In addition, the paper highlights the potential future uses of the technology; the pitfalls to avoid when considering its use; when and how legislation and regulatory policies come into play; and how the technology is evolving and growing stronger (some say that the fourth generation of the blockchain evolution is on the horizon!). The paper also discusses parallel developments in quantum computing, its potential impact on blockchain technology, and what developments are in progress to ensure a stable and provably secure, quantum safe alternative to the existing blockchain approaches.

Keywords: blockchain technology; cryptocurrency; cryptography; digital time-stamping; distributed ledger technology; hash; IUPAC; proof-of-concept; scientific research workflow; trust; quantum computing.

Executive Summary

At the 2019 Council meeting of the International Union of Pure and Applied Chemistry (IUPAC) members requested that IUPAC shed some light on the scientific applications of blockchain technology. The request was reinforced in 2021 when blockchain was identified as one of the top 10 emerging technologies in chemistry by IUPAC and a number of blockchain start-ups in chemistry were established. Nevertheless, blockchain technology has not been widely adopted across scientific disciplines including chemistry – the life sciences appear to be the most advanced in its use.

As a result of both the IUPAC member request and the positioning of blockchain technology in the emerging technologies top 10, this white paper was developed. Its main goal is to present an objective overview of the

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current use of blockchain technology along the scientific research workflow and in related areas such as chemical/drug supply chains and education. It should be noted that blockchain is one example of distributed ledger technology (DLT)[1] that is a record of consensus with a cryptographic audit trail maintained and validated by nodes. The ledger can be either centralized or decentralized and while blockchain is one way of implementing a DLT, not all DLTs employ blockchain.

This paper is the culmination of three years of data gathering, including input from multiple interviews with pioneer users of the technology, as well as from more recent adopters and industry technology analysts' reports.

You will find within these pages descriptions of successful applications of the technology at each step of the scientific research workflow – from the timestamping of ideas to funding, to actual experimentation, to the analysis of research results, and ultimately to the sharing of information and the publication of results. Many of these applications have resulted in major labor efficiencies and cost savings, especially on the administrative side. For example, the U. S. Department of Health and Human Services (HHS) uses blockchain technology to manage their grant program more efficiently and has been able to reduce the time required to complete grant assessment tasks from four-plus hours to 15 minutes.[2] HHS also uses blockchain technology to lessen the time required to find the best deal for purchases of equipment, clinical tools, etc. While this regularly could take four to five months, their blockchain-based service allows people to find what they need in real time and resulted in a contract that will save the government $30 million U.S. dollars over a five-year period.[3]

However, not all blockchain use cases have such a successful conclusion. In this white paper you will learn where the technology has not worked – and why – thanks to those interviewed who discussed in detail the lessons that they themselves learned during their own blockchain journey. The paper highlights the potential future uses of the technology; the pitfalls to avoid when considering its use; when and how legislation and regulatory policies come into play; and how the technology is evolving and growing stronger. The paper also discusses parallel developments in quantum computing, its potential impact on blockchain technology, and what developments are in progress to ensure a stable and provably secure, quantum-safe alternative to the existing blockchain approaches.

One of the key goals of this paper is to make the distinction between blockchain technology and cryptocurrency very clear. The two are quite separate entities. Blockchain is *not* cryptocurrency – it is the underlying engine that supports cryptocurrencies. More significantly, it is an engine that supports a diverse array of use cases across many industries and predates the emergence of the Bitcoin cryptocurrency by almost 20 years.

Another key goal is to encourage everyone who works along the scientific research workflow to learn more about blockchain technology and question if/how it might be of value to them now or in the future, for we believe that it is a proven, potentially-disrupting, technology that should not be ignored.

Introduction: technology – the driver of change

Technology has the power to change the way we work and the way we live. For example, before the onset of the COVID-19 pandemic, how many of the world's population were familiar with videotelephony (the technological underpinnings of services such as Zoom, Go-to-Meeting, Webex, etc.). Indeed, how many were using the technology almost daily as we are today? Nevertheless, as the world returns to in-person meetings, these services appear to have forever transformed how we work, interact, and come together to collaborate.

While not used so intensely, these services were available well before the pandemic. What catalyzed their adoption was *a common need* – to be able to do business as close as possible to usual in a world turned upside down. Indeed, transformative technologies often emerge from a community of users who have a specific, common need. Members of that community are passionate about the technology itself, understand how it works, embrace its values and benefits, and have a clear vision of the potential that it holds for their future. Broad adoption usually comes at a later stage when those outside the pioneer community come to recognize what the technology can do, build on it, and expand its applications to their own specific use cases. These needs also drive the development of the technology, especially its usability!

Consider the internet. It had its beginnings in the early 1960s[4] as a means for U.S. government researchers to share information. It was particularly important to the U.S. Department of Defense who wanted to ensure that it could communicate in the event of a nuclear attack (this was during the Cold War). Ultimately, the Advanced Research Projects Agency Network (ARPANET) – the network that gradually evolved into what we now know as the internet – was developed. It was quite successful, but usage was limited to government workers and certain academic and research organizations who had contracts with the U.S. Defense Department. As a result, other independent networks were created to facilitate information sharing within specific communities of interest. But by the early 1980s a new communication protocol was developed that allowed these diverse networks to come together, interconnect, and "talk." Hence the internet, a network of networks, was born, and has become an integral part of everyone's daily life. It is an infrastructure that has transformed communication and access to information – allowing today's researchers to collaborate on a global scale effectively and efficiently.

The internet is used as an example because in some ways its history and development have similarities with the subject of this paper – blockchain technology – which itself has the potential to transform how researchers communicate and interact. In its current iteration, what is commonly referred to as "the blockchain" is a platform that can be used to support many diverse applications. While this new technology gained popularity because of its use by a community of those interested in cryptocurrencies, specifically Bitcoin,[5] the technology is simply the engine "under the hood" of Bitcoin – an engine that can be used for many other purposes. Indeed, blockchain is to Bitcoin, what the internet is to email – a big electronic system, on top of which diverse applications can be built. Cryptocurrency is just one of many applications,[6] and the technology should not be dismissed because of high-profile cryptocurrency scandals such as the bankruptcy of FTX.[7] In fact, blockchain technology predates Bitcoin. However, the highly successful cryptocurrency use case provided the technology with broad, global exposure and clearly demonstrated the technology's benefits. As a result, blockchain is now used across a wide range of industries, not only by the financial industry with which it has a natural affinity, but also by industries related to pharmaceuticals, life sciences, bioengineering, physics, healthcare, medical devices and lab equipment, education, publishing, etc. – the list goes on.

This paper will focus primarily on blockchain applications that are currently in use along the typical scientific research workflow, but it will also cover applications more broadly in healthcare, the pharmaceutical industry and in higher education. It will also deal with the legal and regulatory aspects of blockchain technology application, as well as the future direction of blockchain technology.

For the purposes of this paper the five stages of the scientific workflow have been defined as (Fig 1):

1) Generating an idea/hypothesis.
2) Seeking funding (if needed).
3) Running the experiment/observing the process.
4) Analyzing the results/providing insights on the outcomes; and
5) Publishing/disseminating/sharing the information with others.

The key objective of the paper is to demonstrate how blockchain technology is currently being used, and its potential to transform the scientific research workflow, including the chemistry workflow. This potentially transformational process has already begun.

But first we address three key basic questions: what is blockchain technology? how has it evolved? and how is it being used now? Then we will look at the current challenges to its use, what needs to be considered *before* investing the requisite time and effort in its adoption, its future potential, and why you should consider its relevance as part of your organization's strategic plan.

Blockchain technology: what is it?

This section is not meant to be a detailed technical description of blockchain technology, just an overview in sufficient detail to outline its possible uses. Like the internet, you do not need to be an expert on its underlying architecture – you just need to know what it can do for you. For those interested in a deep level of detail we

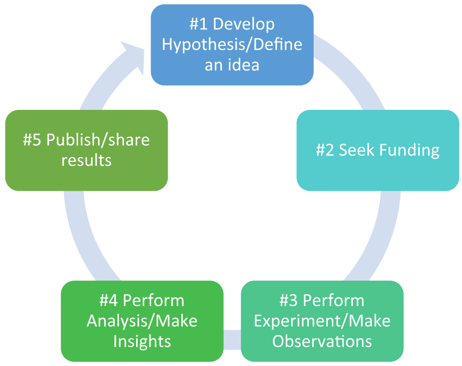

Fig. 1: The scientific research workflow.

provide a reading list in Appendix B. Here we will provide a high-level view so that you can step back and conceptualize how blockchains work *today*. A later section will describe the global efforts that are being undertaken to further improve and enhance the technology and what that means for the future.

As noted earlier, blockchain is one example of distributed ledger technology or DLT. A 2018 article on blockchain in *MIT Technology Review*[8] discusses the technology within the context of the double-entry bookkeeping method[9] that dates to the fourteenth century. That method was established as a reliable record-keeping tool and became an integral part of the business culture, but it also allowed institutions such as banks to eventually become powerful intermediaries in the handling of business transactions – something that continues to this day. Without going into any further great detail on how distributed ledger technology differs from blockchain technology, it is sufficient to say that all blockchains are DLTs but not all DLTs are blockchains (Fig. 2). Moreover, blockchains are specific implementations that use chains of blocks, universally encrypted. DLT, on the other hand, is a broader term that encompasses various implementations, including blockchain, and can offer more flexibility and scalability.

Blockchain is disrupting centuries-old methods of doing business in a global economy.[10] It is a secure, peer-to-peer digital version of the classic double-entry ledger and its inherent features eliminate the need for intermediaries.

The comparison to a ledger is also used in a report on the technology from the U. S. National Institute of Standards and Technology (NIST), which states “Blockchains are immutable digital ledger systems implemented in a distributed fashion (i.e., without a central repository) and usually without a central authority. At its most basic level, they enable a community of users to record transactions in a ledger public to that community, such that no transaction can be changed once published”.[11]

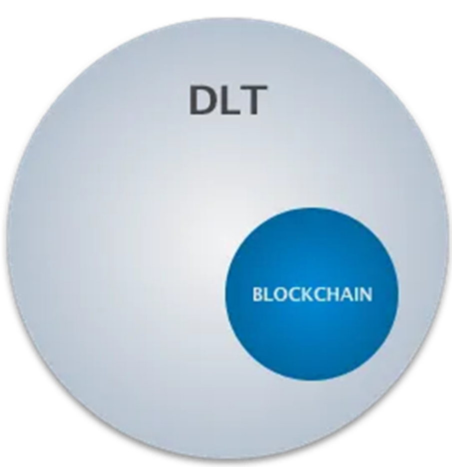

Fig. 2: DLTs vs. blockchains.

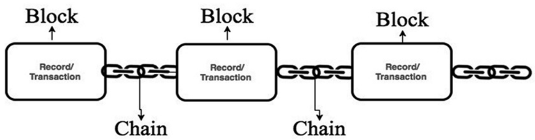

Fig. 3: A visual rendering of a blockchain.

Blockchain's name is related to the way in which it stores transactional data – in blocks that are linked together to form a chain.[12] The blocks record and confirm the time and sequence of transactions, and each block contains a digital fingerprint or unique identifier (a "hash"), time-stamped batches of recent valid transactions, and the hash of the previous block (see Fig. 3).

The hash of the previous block links the blocks together and prevents any block from being altered or a block being inserted between two existing blocks. Each subsequent block strengthens the verification of the previous block and hence the entire blockchain. The method renders the blockchain tamper-evident, leading to the key attribute of immutability.[13] We go into more detail on hashing in Section "Blockchain Technology and Intellectual Property".

If a member of the community makes a change to information on one of the blocks, that block is not altered. Rather, the new information is stored on a new block linked to the prior block, noting that a change has been made on a certain date and at a certain time, allowing information to be tracked – and trusted. The updating process is *not* automatic – there is a consensus verification procedure that must be followed. The two most popular procedures are "proof-of work"[14] and "proof-of stake",[15] the former is used by the Bitcoin blockchain, and the latter was implemented in 2022 by a newer platform, Ethereum.[16] Both require that a cryptographic puzzle be solved before the new block can be added. With the "proof of work" procedure all the "miners" (those who record transactions to the blockchain) use computational power and compete to solve the puzzle. Once it has been solved, the solution is shared with all the other computers on the network that verify (or not) that the solution is correct. If correct, the miner who was the first to correctly solve the puzzle is rewarded. With the proof-of-stake process a miner is chosen randomly to solve the problem from those who have a set "stake" (number of coins) in that blockchain. In both cases, *only* when the solution has proven to be correct is the new block added. For a detailed comparison of these two methods see *Proof of Work* Vs. *Proof of Stake: Which one is Better?*[17]

The MIT article mentioned at the beginning of this section states that one of the key reasons for the technology gaining momentum in its adoption is because the technology itself "…is all about creating one priceless asset, Trust," and it holds the promise of trust even for non-financial "transactions" such as the sharing of data, publishing, etc. According to the *Encyclopedia Britannica*[18] trust can be defined as: "the belief that someone or something is reliable, good, honest, effective, etc." In their early seminal book on the "Blockchain Revolution" (see Appendix B for the full reference), Don and Alex Tapscott state:

"In the emerging blockchain world, trust derives from the network and even from objects on the network… "trust" refers to buying and selling goods and services and the integrity and protection of information, not trust in all business affairs…a global ledger of truthful information can help build integrity into all our institutions and create a more secure and trustworthy world…The ledger itself is the foundation of trust."

This fundamental topic of trust is a thread woven throughout all discussions of blockchain technology. The unique combination of the attributes inherent to the technology's architecture,[19] and the associated irrevocable social acceptance of these attributes as sources of truth about data, correctness of actions, and validity of contracts, result in the creation of trust. This makes blockchain ideal to support many of the activities intrinsic to the scientific research workflow, particularly regarding data management and governance.[20] These attributes are as follows:[13]

– *Distributed/decentralized/sustainable*: Blockchain participants are physically removed from each other and connected via a computer network. They have control over their personal identity and can share at minimum only the information required to complete a transaction – more if they so wish. Each participant that operates a full node maintains a complete copy of the ledger. These nodes are the computers used by participants to run the consensus algorithms that verify and approve transactions. Because the blockchain is not owned or

controlled by any single organization, the blockchain platform's continued existence is not dependent upon any individual entity. Theoretically, there is no limit to the number of full nodes on a blockchain platform.
- *Immutable:* Completed transactions are cryptographically signed, timestamped, and sequentially added to the ledger. Records cannot be changed unless participants agree and the proper procedure (the "proofing" discussed earlier) is followed.
- *Transparent and auditable*: Because participants in a transaction have access to the same records, they can validate transactions and verify identities or ownership without the need for third-party intermediaries.
- *Consensus-based*: All relevant network participants must agree that a transaction is valid. A consensus mechanism operated by each full node in the network verifies and approves transactions (note that each blockchain network can establish the conditions under which a transaction or asset exchange can occur).
- *Secure*: Permissions and cryptography prevent unauthorized access to the network and ensure that participants are who they claim to be. Blockchain uses technologies such as public and private keys to securely record the data in the blocks.[21]

It has been said that "blockchain does not eliminate the need for trust. It represents the emergence of trust in a new form"[22] in today's digital world because of its attributes. The value of these attributes to the scientific research workflow will become more apparent when we look at how the technology is being implemented (Note: Several of those that we interviewed stressed that one of the lessons learned is that users must trust the technology provider and that the onus is on the platform developer to educate and to ensure that all stakeholders fully understand the infrastructure and how it works – including the governance of the blockchain).

Blockchain technology: a brief history

To fully understand how the technology works today it is valuable to understand its evolution. As noted earlier, while blockchain technology serves as the foundation for Bitcoin, it predates that cryptocurrency by almost two decades. It was co-invented in 1991 by Stuart Haber and W. Scott Stornetta, both of whom worked at Bell Communications Research (Bellcore) and were attempting to ensure the integrity of digital records via time-stamping. They believed that the ability to certify when a document was created or last modified is essential for resolving conflicts over things such as intellectual property rights.

Their initial efforts involved working on a cryptographically secured chain of blocks such that no one could tamper with the timestamps of documents. Within a year they upgraded the efficiency of their system by incorporating Merkle trees,[23] enabling the collection of more documents on a single block.[24] The Merkle trees created a series of data records, each connected to the one before it. The newest record in the chain would contain the history of the entire chain, making it more efficient by allowing several documents to be collected into one block.[25] Timestamping even today remains one of the more common applications of the technology.

Haber and Stornetta left Bellcore in 1994 to establish a spin-off company, Surety, which in the past provided time-stamping services based upon their algorithms and was the first company to provide commercial blockchain-based services.[26]

Things remained quiet on the blockchain front until 2008 when Satoshi Nakamoto released a white paper entitled, "Bitcoin: a peer-to-peer electronic cash system," which proposed a system of electronic transactions that did not require a reliance upon trust – the middleman (e.g. bank) was removed.[27] Haber and Stornetta's seminal paper, "How to Time-Stamp a Digital Document,[28]" is referenced in the Bitcoin white paper as are two additional papers of theirs and one by Ralph C. Merkle[29] (father of the Merkle Tree). No one knows anything about Nakamoto – whether it is a single person, or a research group and he/she/they left the Bitcoin community in about 2010, leaving blockchain technology development in the hands of those passionate about the technology – computer scientists, cryptographers, and mathematicians around the world.[30]

Over the decade and a half since Nakamoto built upon Haber and Stornetta's work there have been a series of enhancements to blockchain technology, primarily driven by the realization which emerged around 2014/2015 that the technology did *not* need to be tethered to Bitcoin – it could be used for all sorts of cooperative efforts between organizations – including scientific research. This separation of blockchain from Bitcoin was supported by the launch of a new public blockchain in 2015 called Ethereum.[31] It was developed by Vitalik Buterin, an initial contributor to the Bitcoin codebase, who believed that a blockchain should be multifunctional and not just do one thing very well. In his own words "Ethereum is a blockchain with a built-in programming language…the most logical way to build a platform that can be used for many more kinds of applications".[32] With Ethereum, users can record assets other than cryptocurrencies, e.g., data, publications, etc. It is a platform for the development of diverse decentralized applications. One of the innovative features of Ethereum is that users can create a "smart contract" – "a self-executing contract with the terms of the agreement between buyer and seller being directly written into lines of code. The code and the agreements contained therein exist across a distributed, decentralized blockchain network. The code controls the execution, and transactions are trackable and irreversible. Smart contracts permit trusted transactions and agreements to be conducted among disparate, anonymous parties without the need for a central authority, legal system, or external enforcement mechanism".[33]

The launch of Ethereum captured the interest of entrepreneurs who were quick to see its potential. During the period between 2015 and 2018 significant investments in product development were made in the haste to launch new blockchain-based products and services. But over time it became apparent that the Ethereum blockchain had some weaknesses, especially regarding scalability, speed, and cost. As a result, a multi-phase launch of Ethereum 2.0,[34] now known as Ethereum Merge, commenced on December 1, 2020 and the first version was released in September 2022.[35] More developments and upgrades are expected over the coming years, to mitigate or eliminate the aforementioned weaknesses. Blockchain experts interviewed for this paper believe that this change will accelerate the technology's adoption and that the blockchain global landscape will be transformed in two to five years.

It should be noted that in the same year that Ethereum was launched the Linux Foundation established Hyperledger, a global open-source community focused on the development of stable frameworks, tools, and libraries for enterprise-grade blockchain implementation.[36] Their blockchain differs from Ethereum in that it is a private blockchain, not a public blockchain. A public blockchain or permissionless blockchain is a type of blockchain that does not require permission from any centralized entity or any intermediary. It is decentralized. While a private blockchain has selective decentralization or degrees of centralization. Organizations will choose one over the other depending upon their comfort zone regarding their specific use case.

Both public and private blockchains are thriving today because they each have their own strong user communities. The blockchain landscape today is not unlike the early days of the internet when several networks around the world co-existed in parallel but could not talk to one another. Blockchain interoperability is essential to the future adoption of the technology and technological inroads are being made to make this happen in the foreseeable future.[37,38] Currently there are several blockchain networks that offer interoperability solutions to other blockchain networks. The most prominent include Polkadot,[39] Cosmos,[40] and Harmony,[41] and this topic is re-visited later in this paper in Section "The Present and Future of Blockchain Technology: Technical Capabilities and Challenges" on the future of blockchain technology.

As of this writing it is generally agreed that the future of blockchain technology looks bright. The scope of its impact is hard to predict as it is in the early stages of broad adoption. According to Gartner, Inc., a market research company that follows the rise (and fall) of technologies, "The evolution of blockchain cannot be ignored…The impact of the technology will be significant".[19] Furthermore, at the 2023 World Economic Forum in Davos, it was stated that "blockchain as a technology will continue to grow exponentially and its use cases expand. The real-world applications of blockchain … offer far greater utility and cost savings".[42] So let us look at some of the innovative ways that blockchain technology is currently being applied along the scientific research workflow.

Blockchain applications along the scientific research workflow

As noted earlier (Fig. 1), we have defined the scientific research workflow as follows:

1) Generating an idea/hypothesis.
2) Seeking funding (if needed).

3) Running the experiment/observing the process.
4) Analyzing the results/providing insights on the outcomes; and
5) Publishing/disseminating/sharing the information with others.

This workflow mirrors the one presented by Sean Manion, Chief Scientific Officer, Equideum Health, and Editor for the journal, *Frontiers in Blockchain*, during our interview with him. He had an additional step regarding the identification of the regulatory issues that need to be considered as he is very much involved in clinical trials. You will learn more from him in Section "Blockchain Technology Applications in Healthcare and the Pharmaceutical Industry" where we discuss blockchain applications in Healthcare and the Pharmaceutical Industry. Note that the range of blockchain applications per step varies as the technology continues to evolve, driven by the more compelling use cases (Note: the artwork in this section was generated by the free Artificial Intelligence-based engine Craiyon[43]).

Step #1: develop hypothesis/define idea

The chief application for this step is the timestamping of an idea or hypothesis once it is posted on a blockchain via a hashtag. This was the first application of blockchain and the force behind Haber and Stornetta's blockchain technology development to certify when a document was created or last modified so that conflicts over things such as intellectual property rights could be more easily resolved.

Since timestamping was the first blockchain application, it is logical that there are several organizations who offer such a service. In alphabetical order, here is a sampling of the organizations who are active in this space as of this writing:

ARTiFACTS

Based in San Diego, CA (USA) ARTiFACTS[44] launched a range of services in 2018 – from the timestamping of research through to data sharing and publication. It is the first blockchain-based service for securing provenance (via timestamping) of unpublished and hidden research evidence, making all work eligible for formal citation recognition and impact reporting. It is well known that databases such as the Web of Science, Scopus, and others mainly focus on peer-reviewed, published literature and exclude valuable research materials that are either never published or underpin published works. The co-founders of ARTiFACTS saw that blockchain technology had the potential to enable all types of research materials to be indexed at low cost and in ways that created greater incentives for scientists to share their work earlier – so long as they could be acknowledged for their contributions.

ARTiFACTS uses the blockchain developed by the Bloxberg Consortium that was founded by the Max Planck Society[45] (see Section "Bloxberg Consortium"). They had evaluated other blockchains and settled on Bloxberg because it was created and operated by trusted research organizations for the purpose of testing and deploying services across a blockchain used for science.

The company's initial service for curating ancillary scientific material attracted a core group of active researchers and was adopted by several innovative publishers to augment their citation footprint. Made available to individual researchers at no charge, the service continued to attract registered users and interest across the scientific research community. The co-founder of ARTiFACTS, Dave Kochalko noted, when interviewed, an attractive feature of this service was that ARTiFACTS cannot see the information that is maintained in private mode. He also explained that the system does not put the data files researchers create onto a blockchain. Instead, the files are either stored on servers that the user or institution prefers. ARTiFACTS' vision for their future includes connectivity with data storage facilities; capturing data directly from the devices that produce them; automating the addition of metadata to files; more granular events-tracking as events and actions progress through the research workflow; performing core services within the organization's Information Technology environment; and delivering dynamic analytics reporting from its database.

Building on the experience gained by introducing this blockchain-based citation recognition service, the company re-branded its initial service as ARTiFACTS File which continues to be available to registered users, and has embarked on a new path with its launch of ARTiFACTS VERIFY.[46] VERIFY is a platform designed to assist in the detection of substandard and falsified (SF) drugs at all stages in the pharmaceutical supply chain. VERIFY fills an important gap in safety and regulatory practices. Through the company's collaboration with the Lieberman Lab at the University of Notre Dame, ARTiFACTS VERIFY is used to capture-track-analyze the data associated with chemical analysis of medicine samples. Securing these data to blockchain creates an immutable chain of custody, the outputs of which provide actionable analytics that target SFs and contaminants *in situ*, support active scientific research programs, and identify emerging risks to commercial supply chains. The VERIFY platform is well advanced toward achieving its product vision of a commercial scale solution as of this writing, having demonstrated product viability for generic antibiotics and chemotherapy medicines collected and initially screened in Africa. An extension of ARTiFACTS VERIFY is being considered to support harm reduction programs in the U.S. focused on identifying contaminated street drugs. Such programs are conducted in collaboration with regulatory and law enforcement authorities to monitor the spread of these products and reduce the incidence of mortalities as well as other adverse outcomes.

Kochalko said these are early days for blockchain technology in scientific research and making these capabilities a reality will require more experimentation, deployment of proof-of-concept services, broader engagement by the academic and industrial research communities in the creation of standards and best practices, and expertise in bringing technologies used in finance and big data, such as Machine Learning, to address commercial needs. He expects some of the first areas where we can expect to see things come together is where organizations overlap in ways that require greater trust and transparency, such as with scientists working in clinical research hospitals, regulatory agencies which oversee that work, and pharma companies seeking to move discoveries into actual use as well as protect their intellectual property.

Bernstein

Bernstein is a company based in Munich, Germany that uses blockchain technology to provide secure solutions for the management of Intellectual Property (IP) assets. The company issues blockchain certificates proving the existence, integrity, and ownership of documents or any other form of digital asset. Files are registered on the blockchain of Bitcoin using Bernstein's protocol, which inserts a digital fingerprint of the work in a time-stamped record that can be presented in courts to support any claim related to IP assets or used as a convenient reference in contracts. By using Bernstein, companies can establish a "private trade secret inventory, a measure that is considered a "reasonable step" to maintain confidentiality and therefore fulfills this requirement under the EU Trade Secrets Directive and equivalent." They provide fee-based services for individuals, companies, IP law firms, and start-ups, and you can sign up and try it for free.[47]

Bloxberg Consortium

The Bloxberg Consortium falls under the umbrella of the Munich, Germany-based Max Planck Society (MPS), a group of 86 research institutes – chemistry, physics, the humanities, etc. and their core strength is basic research.[48] The MPS has four central Information Technology service units, one of which is the Digital Library that is responsible for license management, publisher contracts, and the software/technology infrastructure that the MPS researchers and their collaborating partners require. Dr. Sandra Vengadasalam, deputy head of the

Digital Library, became increasingly aware that the researchers at the institutes were concerned about having their research scooped by others. She was asked if it would be possible to get a timestamp or a water mark on their research – whether it be their hypothesis that is written on a piece of paper, lab data such as microscopy outcome tests, and even prepublication information.

As a result, in 2017 her team decided to look at blockchain technology as a possible answer to the researchers' question. They initially looked at Bernstein (noted above) and the Bitcoin blockchain,[49] but decided that because of their commercial nature these might have a negative association in the research community. They decided to build their own platform with the assistance of other founding organizations and their initial use case was timestamping as a proof-of-concept/proof-of-work. They later migrated to an efficient, lower-cost proof-of-authority model. They contacted between 60 and 70 research organizations, and they were able to recruit eleven co-founding research facilities from 10 different countries who joined forces in February 2019 and started work on the project. At that time, the consortium was composed of the following 11 members: Carnegie Mellon, University College of London (UCL), ETH Library at the Eidgenössische Technische Hochschule, the Swiss Federal Institute of Technology in Zurich, Georgia Tech, IT University of Copenhagen, University of Belgrade, University of Johannesburg, University of Basel, University of Nicosia, University of Sarajevo, and the Max-Planck-Gesellschaft. This group signed the Bloxberg Manifesto on February 20, 2019[50] and since have grown to more than 50 members despite the COVID-19 pandemic.

During an interview with Dr. Vengadasalam and James Lawton, who at the time was the technical lead for the project, they noted that because of the Digital Library's activities in Open Access publishing their vision is to change the publication system, and consequently the next use case that they are tackling is peer review. She added that there are other applications in the research life cycle that would benefit from the openness and transparency that blockchain technology offers such as funding, data sharing and aggregation, etc. Indeed, the Bloxberg team believes that blockchain can enable a re-imagination of the research life cycle. She noted that on the administrative side, certification of theses, examinations, and degrees is another use case. Overall, the Bloxberg Consortium appears to be emerging as an important "blockchain for science" with its aims to foster collaboration among the global scientific community, empowering researchers with robust, autonomous services that transcend institutional boundaries. Organizations who do not want to build their own platform can utilize Bloxberg's if they sign the Manifesto and abide by the governance rules. Commercial entities can also join the consortium, but they cannot serve as authority nodes. For more information consult the most recent version of the Bloxberg white paper.[51]

It should be noted that at the fourth Bloxberg Summit meeting held May 4-5, 2022, more than 25 research organizations decided on several proposals regarding the future development of the Bloxberg network. With the first vote, the consortium made a groundbreaking decision, introducing a significant and forward-looking change for the future of the network: the "Bloxberg Association for the Advancement of Blockchain in Science" which was founded under German legislation that same year. Refining Bloxberg's governance model followed this proposal. In the third decision, the consortium agreed to introduce tokenomics to Bloxberg to ensure sustainable funding of the infrastructure. Finally, the consortium members supported a technical proposal to move from a monolithic to a modular architecture with the current Bloxberg infrastructure as Layer1.[52] It appears that the consortium has strengthened considerably since its launch just a few years ago.

Proof of existence

Developed in 2014, Proof of Existence[53] provides a decentralized service that allows users to store an online distributed proof of existence anonymously and securely for any document. Like ARTiFACTS, the documents are not stored in their database or on the bitcoin blockchain. What is stored is a cryptographic digest of the file, linked to the time at which the user submitted the document. In this way, he/she can later certify when the data existed. The service is fee-based, and payment is made via Bitcoin cryptocurrency.

Stampery

Based in Madrid, Spain, Stampery[54] provides a blockchain-based service that via timestamping offers proof of existence, ownership, and data integrity, and facilitates the sharing of data with proof of receipt by the designated recipient. Blockchain-based, the service is secure, transparent, private, verifiable, and auditable. For more information read the Stampery white paper[55] that was published in October 2016 and describes their technology.

Step #2: seek funding (if needed)

Ironically, since blockchain technology in more recent years has risen in prominence because of Bitcoin and cryptocurrency, it is not widely used as a funding mechanism for scientific research…. *yet*. There were some initial players that emerged in 2017–2018, for example Scienceroot,[56] KnowbellaTech, ArnoGenomics, etc., but they seem to have either disappeared or have changed their business objectives. That said, there are a few examples of companies with funding platforms (the DEIP, Matryx, and Molecule approaches are outlined below). An even stronger example of the use of blockchain technology to manage the federal funding/grant processes efficiently and cost-effectively is described in Section "Project: Grant-recipient Digital Dossier (GDD)" on the U.S. Health and Human Services Grant-recipient Digital Dossier project, GDD.

DEIP

When we first encountered DEIP and their Decentralized Research Platform, they were very much focused on the first step of the scientific research workflow. They described themselves as a blockchain-based ecosystem totally focused on the protection, evaluation, and exchange of digital assets. At that time, they claimed to be able to store time-stamped proof-of-authorship and ownership to an immutable distributed register so that scientists could have proof of their contribution, and they appeared to offer a platform for the crowd-sourced evaluation of ideas under consideration by experts in the field. The URLs to those activities are no longer live. However, they did study scientific researchers to learn more about the needs in the scientific research workflow and they identified several areas where they believed that blockchain technology could make a difference. These included research crowdfunding, evaluative tools for funding agencies, and funding of creative works.

Since then, it appears that their main focus has been the development of a technology infrastructure and an economic model that they term the "creator economy," a blockchain-based economy such that "creators can create content, publish, and share content with their followers, and get paid directly for their work."[57] Alex Shkor, DEIP Co-founder and CEO, describes DEIP as the "first web3 creator economy protocol with a mission to help realize the creative potential of humanity and bring millions of creators to web3".[58] He said that they are "building a global system", where creators will be able to monetize their IP in a much simpler and efficient way. They imagine a patent system that works for any asset, from fashion shoe design to the next compact nuclear reactor. Their system is global by default, and it takes just a couple of minutes and a couple of dollars for a person to register their IP. It will allow people from all over the world to create freely and monetize their work in a global market. DEIP is taking care of the requisite underlying infrastructure. Their core innovation is attaching the actual ownership of an IP asset to a non-fungible token (NFT). An NFT is a digital certificate of authenticity stored on a blockchain, which verifies the ownership, authenticity and uniqueness of a particular asset. NFTs are distinct from interchangeable or replaceable assets, which are known as fungible tokens, e.g. dollar bills and bitcoins.[59]

DEIP have an interesting history,[60] have attracted investors, and have several projects[61] building on their vision. The basic time-stamping that they began with must be an essential part of the "plumbing" of their current ecosystem and it will be interesting to see how it plays out.

Matryx

Matryx is an open-source platform for the crowdsourcing of collaborative research with a tokenized reward system that was developed by Nanome,[62] a company that is focused on using virtual reality (Oculus™) in scientific design, e.g., drug design, molecular design, etc. Tokenization refers to a process by which a piece of sensitive data such as a personal identifier is replaced by a surrogate value known as a token. The original sensitive data needs to be stored securely for subsequent reference but tokens themselves have no intrinsic meaning. Tokens are frequently generated by use of one-way cryptographic functions (e.g. hashing) to ensure irreversibility. Tokenization differs from encryption in that the token is usually of similar structure and format to the original data. Tokenization is often used in credit card transaction processing.[63] The concept behind Matryx is that problems can be posted on the platform along with a bounty for a verified solution. Users then collaborate to solve the problems. When interviewing Steve McCloskey, a Nanome Co-founder, he said that he is uncertain how many people are using the platform. He added that when they built Matryx they thought it might be a way for graduate students to make money on the side while helping to find a cure for a specific disease and perhaps even land a job when they graduate. But since blockchain is a new technology, he believes that the majority of people do not understand its value. He said that where the research community is today with this technology is not where it will be in the not-so-distant future. Nanome plans to embed blockchain in the backend of their virtual reality application so that when a researcher uses the app to design a molecule it will be automatically hashed on a blockchain and timestamped as indisputable proof of provenance. For more information on Matryx consult their 2019 white paper.[64]

Molecule

Molecule is building a global system that finances and curates the most promising therapeutics. Their goal is to "turn therapeutic Intellectual Property (IP) into a liquid asset class that allows for new interaction forms around research data, with a goal to create new incentives for collaboration, funding, and licensing of technologies by changing the way that we interact with intellectual property".[65] In August 2021 they announced that their first university biomedical intellectual property research project was funded as an NFT (non-fungible token[66]), enabled by a pioneering innovation at Molecule in partnership with VitaDAO. They said that "the IP-NFT enables new fundraising and collaboration strategies for researchers by combining legal and technical frameworks with NFT technology. Early-stage research can be financed without endless grant applications, creating a startup, and raising Venture Capital or needing to file a patent".[67] On August 2nd, 2022, they announced that they will be funding drug discovery research based in the United States for the first time and it will take place at the University of Washington in Seattle.[68]

Uses of blockchain technology on the administrative side of funding have emerged. The U.S. government has an initiative to manage the federal grant programs more efficiently and transparently from start to finish. This was undertaken because of the huge success of the Accelerate initiative of the U.S. Health and Human Services (HHS) that uses blockchain technology to lessen the time required to find the best deal for purchases of equipment, clinical tools, etc. Such a search regularly could take four to five months, but with Accelerate people can find what they need in real time. This was the first blockchain-based program in the U.S. Federal government to get an Authority-to-operate and in February 2020 it resulted in a contract that was estimated to save the government $30 million U.S. dollars over a five-year period.[3] Its success garnered a lot of attention in the blockchain community, but now it is just part of the system and shows how a successful blockchain implementation becomes an integral tool and fades into the background.

Project: Grant-recipient Digital Dossier (GDD)

After the success of Accelerate, HHS almost immediately initiated a pilot, the Grant-recipient Digital Dossier (GDD) project, to manage their grant program more efficiently. A 2020 report stated that HHS has the largest U.S. government grants portfolio, overseeing approximately US$500B of US$700B in federal grants funding each year. However, the system at the agency was inefficient due to outdated Information Technology systems and dependence upon paper-based processes.[69] As of July 2021, GDD had reduced the time required to complete grant assessment tasks from four-plus-hours to a fifteen-minute process.[2]

Almost in parallel, the U.S. Fiscal Service's Office of Financial Innovation and Transformation (FIT) decided to determine if blockchain might streamline the complicated and time-consuming grants administration process. Starting in the summer of 2019, FIT and the U.S. National Science Foundation (NSF) launched a proof-of-concept to better understand if blockchain technology might lessen the burden on federal grant recipients because of its ability to provide near real-time visibility when assets are transferred over a blockchain network. Their report was expected to be released at the end of 2021,[70] but we were unable to locate it.

Step #3: perform the experiment/make observations

It is in this area of the scientific research workflow that the inherent features of blockchain technology are invaluable. Consider what information can be captured in this step and how posting it to a blockchain can make research transparent and reproducible.

Who did the experiment? The digital identity and signature of the researcher(s) can be hashed to a blockchain while maintaining the privacy of the individual(s) involved. In addition, the expertise credentials of the experimenters can be hashed as there are organizations who now use blockchain for the creation of micro-credentials[71] (more about this later in Section "Uses of Blockchain in Higher Education"). As a related, real-life example, Hashed Health[72] and other such organizations were used to ensure that the doctors/nurses who moved from one geographic location to another during the peak of the Covid-19 pandemic had the necessary experience and expertise.

When was the experiment performed? As already discussed, blockchain timestamping is a key feature of the technology – it was the reason for which it was originally developed by Haber and Stornetta, and it plays an essential role in protecting a researcher's Intellectual Property.

What materials/methodologies were used? Details on the exact reagents/animals/people and methods that were used can be compiled and linked via a hash posted to a blockchain to ensure that the provenance is captured. This is a step that facilitates the reproducibility and transparency of scientific research because the information becomes immutable.

What equipment was used? Details on the manufacturer, when the equipment was obtained, its maintenance, prior uses and users, the location of the experiment, etc. can be hashed to a blockchain. Going back to the micro-credentials mentioned above, details on the training/expertise of those using the equipment can also be added to provide a level of confidence in the results that are reported. This use has become important in the healthcare industry and for more information there is an interesting article published in late 2020 that details the adoption of blockchain technology in healthcare.[73]

What data was gathered? The raw data gathered during the experiment is a digital asset that can be stored, shared, verified, etc. and this is a common use of blockchain technology. Once the data is hashed to the chain any tampering would become immediately apparent, because the hash would be different. The immutability of a blockchain adds a layer of trust to the data. For more detail on the storage of "data" on a blockchain – whether that data is a hash of a file or the data itself – see Sections "Blockchain Technology and Intellectual Property and Data Management on Blockchains".

What are the results of the experiment? The results are an outcome of an analysis of the raw data. Again, the methodology can be detailed and posted to a blockchain. Key information may be any software that is used, specific calculations, who did the analysis, where and when the analysis was done, etc.

As of this writing there are several organizations who offer services in support of the experimental phase of the scientific workflow. Among these are:

ARTiFACTS: Already discussed within the context of time-stamping ideas and hypotheses.

Bloxberg Consortium: Already discussed within the context of time-stamping ideas and hypotheses.

Matryx: Already discussed within the context of crowdsourcing of research funding.

Open science chain (OSC)

Launched in 2018, this is a consortium blockchain (like Bloxberg) that is funded by the U.S National Science Foundation (Award 1840218[74]) and is based at the San Diego Supercomputer Center at the University of California San Diego. Its main objective is to support data sharing to enable independent verification of scientific data and to foster data reuse for the advancement of science.[75] They:

i) provide for the timestamping of datasets to provide proof of data ownership;
ii) promote the transparency and traceability of research data by tracking and storing all changes made to the data on a blockchain; and
iii) allow for independent verification of the authenticity of scientific data using information stored in the OSC blockchain.

Users can search, view, and validate scientific datasets, including lineage information, and create "research workflows" linking one or more entries in the OSC blockchain and other repositories such as GitHub,[76] thereby documenting an auditable record of the data workflow process behind the research hypothesis. The project has been successful and, in the summer of 2021, received an additional half million dollars from the NSF for expansion.[77] The service is free to members of the academic and research communities. For more information about the OSC mission see its seminal paper.[78]

Step #4: perform analysis/make insights

The next step in the scientific workflow process involves taking the results from the experiment performed in Step #3 and performing one or more calculations, analyses, and visualizations on that data to generate conclusions, make insights, and to guide the next stage of the experimental discovery cycle.

In many respects "perform analysis" is like the "perform experiment" in Step #3, except that the analysis experiment is performed without tangible or physical materials or equipment – unless one calls pen and paper, or a PC, equipment! For the purposes of this article, we have assumed that "perform analysis" means executing *in silico* (i.e., using a PC and analytical software) an operation or an algorithm on experimental data that is generated *in vitro* or *in vivo*. In other words, Step #4 takes the data generated in Step #3 and uses computational processes to generate more results, again in the form of data, which supports, or not, the experimenters' initial hypothesis. In the Step #4 *in silico* experiment, we have to all intents and purposes, the same "actors and artefacts" as we had in Step #3, namely: (i) the person who ran the analysis (the "who"); (ii) the methods that they used (the "how"), which in this case comprises the software, algorithms, and mathematics that they used; and (iii) the results, observations, and conclusions that they generated. And just as in step #3, there are tools to help these *in silico* experimenters or "informaticians," to capture and manage the metadata around the experiments that they run. Perhaps the most widely-used of these informatician tools is the Jupyter notebook.[79] The Jupyter notebook is an "open-source web application that can be used to create and share documents that contain live code, equations, visualizations, and text".[80] While it does not have blockchain technology embedded within it, a Jupyter notebook can quite easily be connected to, for example, an Ethereum node to deploy a smart contract.[81] Note also that there is a new Electronic Laboratory Notebook (ELN), Labii,[82] that uses blockchain to secure research data. In addition, in 2021, the National Institute of Standards and Technology (NIST) funded a research project for the development of a prototype Digital Research Notebook system called KnowLedger. The concept for this new ELN is to build a system where research data is captured semantically immediately at birth and stored on a blockchain, and updated incrementally as knowledge is added. This initiative is the brainchild of one of the authors of this blockchain white paper, Dr. Stuart Chalk (see Appendix A for more details).

But why might one want to involve blockchain technology in *in silico* analysis? Because the technology's main value rests in its transparency, immutability and auditability, disintermediation, and trust enablement. If the data that result from a physical or *in silico* experiment have, by some mechanism, been registered or captured on a blockchain (e.g. by storing a hash of a data file), then whoever takes that data file and performs an analysis on it can have a higher degree of confidence that the results they generate can be traced back, or audited, to an immutable, time-stamped dataset (as fixed by the hash). In other words, if the informatician, whose role is now increasingly being called "data scientist," also captures their results and methods on a blockchain, they can now demonstrate a clear line of sight (akin to a data family tree[83]) back to a starting dataset. This trusted auditability and integrity enabled by blockchain technology is being viewed increasingly as a compelling use case by data scientists,[84,85] so much so that some commentators are now saying that "data science and blockchain are made for each other".[86]

Putting this axiom aside for now, it is perhaps more important to recognize where blockchain-enabled data analysis can have genuine real-life benefits and utility. In our view, wherever the conclusions and resultant actions from an experiment need to be unequivocally and irrefutably linked to a dataset which resulted from that experiment, then blockchain technology can play a significant, value-adding role. One primary example would be in the GxP (Good Laboratory/Manufacturing/Clinical Practice) area of drug discovery (for more on GxP see Section "Blockchain Technology and GxP: Enabling Adherence to Regulations" that covers legal and regulatory considerations). In this highly-regulated domain, the effective and immutable capturing of experimental data, the analyses that are performed on that data, who performed those experiments and where, and the ultimate conclusions on that data, all of which together may decide whether a drug is suitable (safe and effective) for human consumption, could be made more reliable, more secure, and more transparent if those data and metadata were captured on a blockchain. Currently, if such data lineage is being captured using DLT we, the authors, are not aware of it. But if data analysis, data science, and blockchain technology are truly "made for each other," the GxP domain could be one area where that statement is proven correct.

Step #5: publish/share results

Steps one, three, and four create the content that can be shared on a blockchain if desired, and/or submitted for publication to be made available to the global scientific community. There are several diverse players in this space that offer publishing/sharing services via blockchain, some of whom could potentially disrupt the traditional publishing process because of the value that blockchain brings to the table. Current challenges[87,88] in the overall publishing/science communication process are as follows:

- Academia has a “publish or perish” mindset and researchers choose to publish in the top journals for a variety of purposes including tenure (commonly in what are known as “High Impact Factor” journals). As a result, a handful of publishers control most research outputs.
- Access to research findings can be difficult because of the journal subscription model. Access depends on a university’s library budget. Access by the public is even more difficult.
- Research only becomes accessible at the point of publication. Everything that takes place prior to that point – such as collecting and analyzing data, peer review, etc. – is not transparent, leading to reproducibility problems.
- With peer review – the process whereby research papers are evaluated by peers in the same field before a paper is published in a journal – there is lack of visibility, as well as recognition and accountability recognition for reviewers, with their review work remaining largely unnoticed and unrewarded.
- Scientific results are primarily published in academic journals, which have a strong tendency to publish positive and novel results. Scientists themselves are more inclined to report on their successful outcomes rather than on failed experiments. A lot of research that did not lead to positive results, therefore, remains unpublished and unknown – possibly leading to more time, effort, and funding being spent on similar efforts.
- Publication cycles can be lengthy.
- Scientific “misbehavior” such as plagiarism, tampering with research results, etc., unfortunately does happen.

While there is no technological solution to the first two challenges noted above, blockchain technology can help to deal with the others. Players in this step of the scientific research workflow who are using blockchain technology for publishing are aware that the technology promotes transparency, fosters speedy communication, mitigates data tampering and fraud, and can offer rewards (tokens) for usually unrecognized efforts such as peer review. As of this writing the following is a representative sample of the players in this step (in alphabetical order):

ARTiFACTS

As noted earlier, ARTiFACTS was the first blockchain-based service for securing provenance (via timestamping) of unpublished and hidden research evidence, making *all* work eligible for formal citation recognition and impact reporting. The limitations in scholarly communication that drove their development of a blockchain system to track negative or confirmatory findings and the significant amount of published research that cannot be verified or reproduced are yet to be fully addressed.[89–91] Although the company currently is not actively pursuing new user adoptions of ARTiFACTS File, independent researchers and publishers continue to experiment and look for ways to differentiate their journals to attract authors and submissions. In these cases, publishers have encouraged use of ARTiFACTS File by their author community. This creates an opportunity to boost the citation profiles of the authors as well as the journal when materials previously not shared can now be cited, counted, and reported on dashboards. As an example, the *Journal of the British Blockchain Association* has collaborated with ARTiFACTS on the world’s first blockchain application specifically designed to enable researchers to create a permanent and immutable public record of research material in real time.[92,93] In an interview for this paper, Dr. Naseem Naqvi, President of the British Blockchain Association[94] and Editor-in-Chief of the *Journal of the British Blockchain Association*,[95] stated that he is a strong supporter of the use of this technology in scientific research because it provides a data audit trail with immutable time-stamps and protects Intellectual Property, especially for pre-published data, articles, etc. as well as published works. He encourages his authors to take advantage of the technology's benefits because at any time they can provide proof of their work. As of this writing another publisher, *Partners in Digital Health*, had also partnered to register each original research article's provenance on a blockchain for every author to create a permanent and immutable public record of their work on a blockchain for the scientific community.[96] Those in the academic research community interested in exploring use of ARTiFACTS File are encouraged to contact the company directly.

The company's current focus on addressing the challenge of identifying and reporting counterfeit medicines in the supply chain continues to pick up momentum. With successful deployments of ARTiFACTS VERIFY tracking the incidence of substandard and falsified medicines in multiple African countries for two important therapeutic drug classes, antibiotics and chemotherapy products, the company is scaling up for commercial uses by healthcare providers. An extension of this system for reporting on contaminated opioids in the U.S. is being considered as of this writing. The delivery of such a service would be in collaboration with harm reduction social service providers under the guidance and authority of public authorities.

Bloxberg Consortium

As noted earlier, Dr. Sandra Vengadasalam, deputy head of the Max Planck Digital Library that is responsible for the MPDL blockchain, has told us that because of their activities in Open Access publishing, their vision is to change the publication system. The next use case that they are tackling is peer review and they announced in 2020 that they have decided to develop a peer review aggregation app which they have since done.[97] They know that the diverse stakeholders in the peer review infrastructure are hesitant to share information back and forth, but with blockchain technology Bloxberg can manage the sharing of information and control access in a decentralized way. Also, mechanisms can be built into the chain to incentivize people to make the effort involved in doing peer review. It is unfortunate that the consortium did not exist when the Blockchain for Peer Review project was launched in 2018. It may have had a different ending (see Section "Blockchain for Peer Review" for more details).

Ledger

Ledger[98] was established in 2015 at a time when research on blockchain technology, cryptocurrency and related topics was experiencing significant growth but did not have a publishing home that offered the peer review function. Since for many academics, their research does not "count" in the eyes of their peers unless it is published in a traditional academic journal, the founders of *Ledger* wanted to make it easier for academics to get their blockchain and cryptocurrency research published in a peer-reviewed journal. They also wanted to raise the standard of research being done by scholars (not necessarily academics) already in the blockchain/cryptocurrency community. So, they set out to create a traditional academic journal devoted to this topic. The name "Ledger" is derived from the term "distributed ledger technology" which is, as noted earlier, a common synonym for blockchain technology. The journal's founders made it clear that cryptocurrencies are not just about money. They are about recording ownership of arbitrary data and facilitating the transfer of that ownership to someone else without the utilization of a central institution, e.g., trading stocks without a stock exchange; transferring the title to a house without a notary/court; filing a patent without a patent office; issuing concert tickets without a ticket office; and time-stamping scientific results/publications. Indeed, the journal has a broad scope – mathematics, cryptography, engineering, computer science, law, economics, finance, and social sciences. It is Open Access – content is free to view (no subscription cost), free to publish (no author fees), and it is published by the University Library System at the University of Pittsburgh (USA). The first call for papers was in September of 2015 for the inaugural issue that was published in December 2016.

Ledger is similar to most journals in that: 1) it publishes three article types: original research, reviews, and perspectives; 2) the Editors handle submissions, find, and contact reviewers (typically three), and make final decisions; 3) there is a single-blind review process (i.e., reviewers know the identity of author, but not the other way around); and 4) there are multiple review rounds if necessary. But the differences from most journals include, amongst others, a transparent review process. Reviews, including author correspondence, are published alongside accepted articles; once accepted, articles are digitally signed by the authors (the journal provides a user-friendly tool for this). Signing cryptographically proves that an article has not been altered; the signed document is time-stamped by the Bitcoin blockchain which cryptographically proves that the article did not exist before a certain time; under exceptional circumstances, authors are permitted to publish under a pseudonym (the demand for this was less than the journal's founders anticipated).

When speaking at a conference in 2017, Christopher Wilmer, the journal's Managing Editor, said that blockchain technology is well-suited to be used in scholarly publishing because it is extremely resilient, tamper-proof, and practically indestructible; there is no single point of failure or cost of operation; and there is an incontrovertible proof-of-publication date, even across countries and institutions whose incentives are not aligned (which is sometimes a point of contention for scientists racing to discover a cure, put forth a new theorem, etc.).[99]

Ledger has grown into its own and it continues to be indexed in Clarivate's *Emerging Sources Citation Index* (*ESCI*). Other journal publishers are also beginning to use the technology as was noted above in the section on ARTiFACTS.

Orvium

Founded in 2018, Orvium[100] claims to be the first open source, decentralized platform for managing a scholarly publication's lifecycle together with the associated data. Using blockchain and artificial intelligence technologies, as well as decentralized storage and big data, Orvium has created a public, traceable, and trustworthy record of the research publication process.

According to its founders, Manuel Martin (CERN), Antonio Romero (Volkswagen DATA: LAB), and Roberto Rabasco (Founder of BooleanCloud), Orvium improves the quality and effectiveness of scientific publishing while returning the benefits of science to society. In December of 2020, Orvium announced a new collaboration with the European Organization for Nuclear Research (CERN) to promote what they term as a "faster, fairer, and more transparent publishing model to support researchers worldwide".[101] The objective of the partnership (Orvium is now considered a CERN spin-off) is to help researchers and institutions to share their work, create Open Access journals, and streamline the peer review process. With the power of CERN's multidisciplinary, open research repository, Zenodo,[102] and CERN's digital repository management system, INVENIO,[103] firmly planted behind the scenes, Orvium has the credentials needed to disrupt what they term an old publishing model dominated by outdated technology and assumptions about how science works. In 2021, furthering its inroads to the disruption of the traditional publishing model, Orvium announced its partnership with Delft University of Technology's Library[104] and collaborates closely with TU Delft OPEN, the university's open access publisher. Together they have created "The Evolving Scholar" – an open access mega-journal for multidisciplinary, community-driven, and open peer-reviewed publications.[105] In one of their blogs[106] Orvium lays out what they perceived to be the benefits of using blockchain technology in publishing, especially with regards to minimizing the challenges presented by the current publishing business model noted in Section "Step #5: Publish/Share Results".

When the work on this white paper began there were several more players in this space, notably DEIP,[57] Pluto[107], Katalysis,[108] Principia,[109] Science Root,[56] Frankl,[110] and Digital Science with their Blockchain for Peer Review project.[111] The latter project was discontinued in November 2019. Of the players listed in the 2018 article that discussed the use of blockchain in publishing,[87] only ARTiFACTS have become a mainstream player (Orvium and Bloxberg did not exist at the time that article was researched and written). The others, except for Pluto and DEIP, appear to have disappeared. An article was published about the Pluto Research Network as recently as November 2021,[112] and while DEIP still appears to have an interest in the intellectual property area of research as noted in Section "DEIP" they have become more focused on the development of an economic model and the requisite technological infrastructure to ensure public and tokenized research funding and assessment with DEIP-based tokens.

However, even though several early players have disappeared or shifted their focus, that does not mean that there is no interest in applying blockchain technology to the scholarly publishing process. In fact, in 2023 a new blockchain-based publishing platform, Scisets,[113] was launched. There is considerable interest in this use case, and you can learn more about the potential that the technology holds in this space in a book entitled “Transforming Scholarly Publishing with Blockchain technologies and AI”.[114]

Blockchain technology applications in healthcare and the pharmaceutical industry

Early in the interview process for the white paper, it became apparent that blockchain technology had found early adopters in the Healthcare sector, including the Big Pharma component. In the December 2020 teleconference with Sean Manion, who was mentioned at the beginning of Section “Blockchain Applications Along the Scientific Research Workflow”, he provided a rationale for this early adoption – and it was mainly because the health care/ Big Pharma sectors have challenges in improving their processes to save time, money, and lives.

First, he stated that the technology offers better science for the researchers in the Healthcare arena. He noted that there are reproducibility issues in that 20 % of U.S. health science research cannot be replicated/reproduced.[115] Blockchain offers improved reproducibility through transparency and an immutable audit trail for research data; better quality data from standardization; improved materials; and increased meta-analysis capabilities. Second, use of the technology can offer cheaper research for funders. He noted that the cost of research is high, and that the return on investment is declining. The U.S. health science arena is spending $30B on non-replicable research.[106] The use of blockchain technology can increase the return on investment for research dollars spent; it can reduce data management costs through blockchain/smart contracts; it can be amplified with Machine Learning/AI; and it can result in cheaper administrative costs (which the U.S. government has successfully proven in grants management as noted in Section “Project: Grant-recipient Digital Dossier (GDD)”).

The third reason that the Healthcare/Big Pharma sector has adopted blockchain technology is that it has the potential to allow researchers to develop life-changing treatments and cures more quickly. He said that on average it can take 17 years for the results of drug research to reach the patient (from bench to bedside)[116] and he estimated that the parallel administrative processes can take two to five years.[117] Blockchain could offer faster time from idea to treatment; improved outcomes with accelerated research and higher quality data; improved tracking of individual contributions allowing for expanded permissioned access of data to more researchers; faster administrative processes [e.g., Institutional Review Boards (IRB), grant reviews].

Sean noted that administrative use cases, although perhaps considered the most boring, can really benefit from blockchain technology. They usually have good data standards and are the easiest and fastest applications to implement, resulting in greater efficiencies and lower costs. He added that Brian Behlendorf, the Chief Technology Officer at the OpenWallet Foundation as of January 2024 and previously Executive Director of Hyperledger as well as Chief Technology Officer at the Open Spource Security Foundation, said that if science implements blockchain right the technology will be like indoor plumbing – an essential foundation that no one notices. Although blockchain can be viewed as boring beyond the cryptocurrency applications, it also can be very effective. This fact was reiterated in other interviews and the reader can only look back at some of the examples discussed in Section “Project: Grant-recipient Digital Dossier (GDD)” in the funding step of the research workflow to see how effective the technology has been in reducing administrative time and cost.

Sean then provided some concrete examples of how the technology is being used in healthcare and we discovered others along the way. The following is only a sampling:

Medical/pharma supply chain

There are several good examples in this area. For example, the U.S. Federal and Drug Administration (FDA) is running a pilot program to help the pharmaceutical industry move toward meeting the 2023 requirements of the Drug Supply Chain Security Act (DSCSA) which requires that the U.S. pharmaceutical industry be able to track legal changes of ownership of pharmaceuticals in the supply chain. The MediLedger Pilot Project, a consortium of leaders from 25 pharmaceutical companies, was accepted into the program with the goal of evaluating blockchain as the solution to the 2023 DSCSA requirements. The pilot is now complete and the resultant solution is now available.[118]

The FDA has also joined forces with the Good Shepherd Pharmacy and RemediChain, two non-profits with the mission of getting unused but still valid drugs into the hands of people who cannot afford them.[119] This is most useful with high-priced chemotherapy drugs where 40 % of the patients die before the drugs that they are using expire. Such drugs in the USA can cost upwards of 30 thousand dollars a month. Both non-profits are small organizations`, but despite their modest beginnings`, both use blockchain technology which works well for heavily regulated industries such as pharmaceuticals to track "medicine transfers" in the drug supply chain. At Good Shepherd Pharmacy, medicine transfers take place when, for example, the family of a deceased cancer patient donates unused medication to the organization. RemediChain then matches those donated medicines with the most appropriate patients in multiple U.S. states. RemediChain, also handles donations from a variety of sources, including individuals and cancer clinics, taps back into the supply chain data and re-creates any missing information, such as manufacturing and expiration dates. The re-creation of the "chain-of-custody" via blockchain technology assures a medication's origin and quality. According to the FDA, "The program is intended to assist drug supply chain stakeholders in developing the electronic, interoperable system that will identify and trace certain prescription drugs as they are distributed within the United States".[119]

A more recent example is the partnership between the Distributed Pharmaceutical Analysis Lab (DPAL) at the University of Notre Dame and ARTiFACTS (an organization mentioned throughout this paper) to develop a prototype solution for tracking pharmaceutical chain-of-custody information in real-time using ARTiFACTS' blockchain platform. The partnership was announced on October 20, 2021, and the press release states that "up to two billion people worldwide lack access to authenticated medicines. The World Health Organization has estimated one in 10 medical products in low- and middle-income countries are substandard or falsified, with some experts estimating monetary losses of between US$70B and US$200B. More troubling is the human cost – two hundred thousand lives are lost per year in Africa because of fake antimalarial drugs alone".[120] Today's efforts to reduce fraud are manual, time-consuming, lack transparency, and have no chain-of-custody. This partnership aims to: 1) make all relevant information directly available online for researchers and regulatory authorities; 2) create a trusted and secure chain-of-custody of drug samples and their metadata; and 3) scale-up across the DPAL participant community. This partnership was mentioned in Section "ARTiFACTS" of this paper where ARTiFACTS was first highlighted under step #1 of the scientific research workflow.

One of the more visible healthcare projects is PharmaLedger,[121] a three-year project involving 12 global pharmaceutical companies and 17 public and private entities including technical, legal, academic, regulatory, and research organizations as well as patient representative organizations. The project was sponsored by the Innovative Medicines Initiative (IMI) and the European Federation of Pharmaceutical Industries and Associations (EFPIA) under the Horizon 2020 program (now Horizon Europe[122]) and had the goal of building a scalable blockchain infrastructure that will support supply chain, clinical trial, and health data use cases. The initial project ended in December 2022 and the project wrap-up has been published. The work continues through the not-for-profit PharmaLedger Association founded in March 2022.[121] Note that PharmaLedger released its first product, electronic Product Information (ePI) in April 2023.[123]

Clinical trials

Another project worth noting is the Pistoia Alliance's Informed Consent project, which sought to demonstrate the value of blockchain technology as part of a decentralized digital identity solution for the informed consent process that is essential for pharmaceutical clinical trials.[124] The two companies involved were AstraZeneca and Novartis. Richard Norman, the Project Manager at the time of our interview, described the traditional informed consent process as follows: an informed consent form (ICF) template is created by the pharmaceutical company and sent to the Ethics Committee for approval. Once approved, the ICF template is returned to the pharmaceutical company, and this is sent to the clinic where individual ICFs are created for each clinical trial participant. The participant is informed of the clinical study and is asked to sign the ICF which then goes to the Principal Investigator (or other authorized person) for countersigning. Once this is done, the individual ICF is returned to the pharmaceutical company for safe storage. He noted that although the high-level look of the informed consent process is quite generic, when you dig down there are variables that make the process quite complex, e.g., the ICFs vary between countries and studies; participants need to be informed and re-consented using an updated and approved version of the ICF following any change to the clinical study protocol; and consent can be withdrawn at any time. It is a manual process, and it takes a lot of time. He added that the process can be digitized, but despite many benefits, eConsent platforms are centralized and this can raise questions around the privacy and handling of participant personal information during and after a clinical study.

The conceptual solution developed through the Pistoia Alliance Informed Consent project implemented key components of decentralized digital identities: Decentralized Identifiers (DIDs), Verifiable Credentials (VCs), and a blockchain registry, BlockSent, enabled participants to provide consent, be reconsented, and withdraw their consent to participate in a clinical trial. BlockSent provided multiple stakeholders – study sponsors, clinics, ethics committees and study participants – with an audit trail of all the transactions during the clinical trial informed consent process. It ensured regulatory compliance and enabled a real-time overview of the approvals and signature process. The project is listed on the Pistoia Alliance website as being completed in 2022 at which time the Pistoia Alliance announced that the organization has a new strategic theme – Empowering the Patient in R&D – and has called for its members to restructure around patient "centricity" based upon what they have learned during the pandemic.[125] Richard Norman has since left the Pistoia Alliance and has said that if the project continues, most likely it will not continue in its present form.[126] A brief summary of their efforts and their current outlook was published online in Drug Discovery World on February 20, 2024.[127]

For more information on this topic note that an article[128] was recently published on the opportunities and challenges of using blockchain in clinical trials and it is an interesting read.

Medical device tracking

In the section on the scientific research workflow (Section "Blockchain Technology: A Brief History"), it was noted that use of blockchain technology is particularly valuable when doing an experiment because all the requisite information for replicating an experiment can be captured – including essential data on the equipment that is utilized. Similar information is essential in hospitals with regards to medical devices that are utilized for patient care. Sean Manion introduced us to a pilot project that was initiated in 2017 between Spiritus Development and Edinburgh Napier University in Scotland to demonstrate the benefits of blockchain technology in tracking medical equipment through their life cycles.[129] The pilot use case was to track the unique device identifiers (UDIs) which are required from a regulatory standpoint for medical devices to improve their traceability.

We interviewed one of the pilot organizers, Susan Ramonat, who noted that medical facilities are concerned about the operating life of medical devices (and other equipment) as they move through the ecosystem from the manufacturer and their upstream suppliers, through distributors who may provide logistical services such as audit inspection. The equipment may ultimately be decommissioned and disposed of. But more often expensive and highly-valued assets, or those reconditioned or repaired, end up at auction and are distributed around the world to underdeveloped countries that have large populations and rely on secondary markets and auctions for their medical equipment. She said that there is a real challenge in bridging across such diverse parties to ensure that they not only know the chain of equipment custody, but also the service history associated with the device. This use case is not unlike the Vehicle Reports offered by CARFAX,[130] a U.S.-based company that compiles the history of an automobile – so providing a portable history which accompanies an automobile showing the history of its routine maintenance and repair, whether it was involved in any accidents as well as in recalls, and what actions were taken. The organizers of the pilot saw an opportunity to have a similar shared registry for medical devices and equipment using blockchain. The blockchain ledger that they created provided traceable, verifiable, and tamper-evident records across an asset's entire lifecycle. It is a shared registry among all parties involved with shared control and governance and includes both physical and digital assets. It facilitates not only tracking, but also ensures that the right level of skills to use the equipment is made known and that all adverse results are noted. The pilot was successful and when we last spoke to Ramonat, the company that emerged from the pilot, Spiritus Partners,[131] had been working with U.S.-based hospitals for almost five years.

When we went to do a follow-up, we found that Ramonat had moved on and that the blockchain service that Spiritus offered appears to have been discontinued. Why? We do not know definitively, but she did say that the pandemic had slowed things down and had mentioned that one of the challenges that they faced was getting participants to share what she termed the *de minimis* amount of information – what needs to be shared to get the transparency and assurance required by all who are involved – a challenge/hurdle that exists for many, enterprise-related blockchain use cases, whether in healthcare or in the conventional corporate world. However, we do know that there is significant interest in such a service. For example, a group of hospitals in Switzerland used blockchain to track medical devices for the very reasons that Ramonat put forth.[132] Also, there is a company in the U.S., Culinda, that provides a medical device tracking service.[133,134]

A relatively recent article[135] highlights the opportunities that blockchain technology brings to supply chain processes in healthcare such as medical device tracking and the delivery of pharmaceuticals from supplier to user. It describes the technology as potentially “transformative” for healthcare processes and is worth a read.

Uses of blockchain in higher education

Degree/document/identity certification

There are several examples of the use of blockchain technology for the certification of scholastic degrees, documents, and even identity. Just as ARTiFACTS’ blockchain application allows researchers, authors, publishers, etc. to post and time-stamp their work, and the Pistoia Alliance’s blockchain platform was developed to certify the informed consent process in clinical trials, institutions of higher learning are using the technology to certify education credentials. In 2016 the MIT Media Lab, together with Learning Machine, came up with the idea of “blockcerts”.[136] This allowed students to establish their own unique identity on a blockchain and when it was time to graduate, they could quickly and easily obtain a verifiable, tamper-proof version of their diploma that could be shared with employers, schools, family, and friends, giving them autonomy over their personal records. While MIT is no longer involved, Learning Machine was acquired in 2020 by Hyland[137] who continue to steward the project and have extended its use beyond higher education to commercial applications, government agencies, and healthcare institutions.

In 2019, the Malaysian Ministry of Education introduced a blockchain platform, E-Skrol, to tackle the rampant use of fake educational certificates being issued by diploma mills.[138] The platform makes it possible to verify the authenticity of Malaysian educational degrees and is available for all public and private universities in the country.

Another example is work being done by the Open University, the O.U., in the United Kingdom.[139] The University was established by Royal Charter in 1969 with the objective of giving anyone, no matter where in the world they lived, an opportunity to learn, and it is a globally-recognized institution. In early 2021 we spoke with Dr. John Domingue, a professor, and the Director of their Knowledge Media Institute. At that time the O.U. had one hundred and seventy-five thousand students enrolled, making it (by student number) the largest university in the UK and one of the largest in the world.

John said that they became interested in blockchain in 2015 mainly for the purpose of accreditation, but they also have other use cases. Their goal is to empower their students, describing them as “self-sovereign students.” He went on to say that the O.U. wants its students to have control over their own individual learning process and that blockchain technology allows the university to facilitate that control. The idea is that students have their own personal data store, which the university configures to store a student’s accreditation data and then everything is verified on a blockchain. The institution that issues the accreditation signs a hash. He noted that the university utilizes “Solid”[140] which is a personal data store technology. John added that the O.U. has several ongoing projects that are blockchain-based. One is QualiChain,[141] a collaborative effort that began in January 2019 to develop a decentralized platform for storing, sharing, and verifying education and employment qualifications. The project conducted pilots in four key areas: (i) lifelong learning; (ii) smart curriculum design; (iii) staffing the public sector; and (iv) providing recruitment and competency management services. It looked at the hiring process across Europe with the goal of adding another layer of transparency using blockchain technology. The project was given its final review in early 2022 and is considered to have been a complete success.[142] We highly recommend that you visit the QualiChain website to learn more. It includes a YouTube overview of the platform's applications for researchers and educators. You might also consider looking at John Domingue's explanation of blockchain technology as well as some of its uses in education along with a video on the Open University's blockchain research.[143]

Identity certification

Like the "self-sovereign student" mentioned in the above paragraph where the student has control over their education-related certifications, self-sovereign identifiers (SSIs), also based upon blockchain technology, allow individuals and organizations to take control over their digital personal/organizational identities.[144,145] With an SSI, an individual or organization can control who can access their information, maintain their identities themselves, use it for verifying their identity online, etc. We are all used to physical IDs, credentials such as cards issued by a government, employer, university, etc. for verifying that the cardholder is a citizen, employee, or student of the organization. These tangible IDs have several issues associated with their production and use, but the biggest one now is that of ID theft and impersonation. Digital IDs are accessible currently by registering for a service with an email address or username and a password. Digital IDs also enable users to leverage third-party login services such as those offered by Facebook or Google. However, digital IDs also have issues, especially when the ID services are controlled and managed by the larger data-leveraging and technology companies. These issues include the fact that users do not have direct control over the sharing of their data and that they face risks due to the vulnerability of the centralized repositories of personal data on the issuer's servers. Privacy is often at risk with third-party login services featuring financial incentives for data collection and storage. Self-sovereign identity involves setting up a highly secure, digital peer-to-peer network between ID issuer, ID verifier, and ID owner. Even the SSI system provider does not have any idea about the exchange of credentials. Therefore, the process of issuing credentials becomes faster, simpler, and a great deal more secure. The self-sovereign identity blockchain characteristics are evident with cryptographic hashing ensuring that SSI credentials are tamper-proof. Examples of SSI system providers are Evernym, who were acquired by Avast in 2021[146] and Spherity.[147] The latter was involved in the Pistoia Alliance Informed Consent Project that was discussed in Section "Blockchain Technology Applications in Healthcare and the Pharmaceutical Industry". Organisations such as the European Union (EU) have also put in place an SSI regulation called eIDAS to facilitate secure cross-border transactions, by establishing a framework for digital identity and authentication. It aims to create confidence in electronic interactions and promote seamless digital services in the EU.[148]

While we have included digital identity here in the section on higher education because the early use was education-related, note that blockchain-based digital identity can also be used along the scientific research workflow (see Section "Blockchain Applications Along the Scientific Research Workflow", particularly steps #3 and #4), to capture the education, experience, and expertise of those doing the experimentation as well as the evaluation of results.

Examples of projects for which blockchain technology was not the solution

During the many interviews that we held with active players in this space, we found that blockchain technology is not always the ideal solution for a specific problem – even when the technology works. There are many factors that can come into play, key among them being legislation, finance, and human bias. Two notable examples, which we would like to describe in detail, are the Blockchain for Peer Review Project and a project that was being conducted by a group within Elsevier's Healthcare Education Group. It may be that the Spiritus and the Pistoia Alliance projects mentioned in Section "Blockchain Technology Applications in Healthcare and the Pharmaceutical Industry" on the use of blockchain in healthcare were abandoned due to legislative or human issues since both projects had proven that the technology worked, and other projects have subsequently supported that finding.

Blockchain for peer review

The Blockchain for Peer Review project led by Joris van Rossum, then at Digital Science, was officially launched in early 2018. The initial participants were Digital Science, Springer Nature, Katalysis, and ORCID. Soon to follow were Taylor & Francis, Cambridge University Press, Kargers, and the Wellcome Trust as an advisor. The goal of the project was to gather information about the peer review process and share it among the participating publishers. They believed that by creating a trusted data store of peer review data they could coordinate the review process, identify reviewers better, and create a trusted and independent data trail of the peer review process, making it more transparent and trustworthy. The process would then become more efficient, transparent, and recognizable (see the paper that van Rossum wrote after announcing the project at the NFAIS annual Conference in 2018[88]). A year later they published a high-level view of the system's architecture,[149] but once the proof-of-concept was completed, the group had to decide about moving onto the next step. On September 5th, 2019, they met in London to debate the issue and in November they announced that they "could do more in terms of collective action to improve the peer review process, but at the same time there is not one large, specific thing they should focus on" and the project was terminated.

We interviewed van Rossum about eight months after that announcement was made to get his view on what happened. He said that his original pitch to publishers regarding the initiative was that the peer review process is the main plus that publishers bring to the publishing process and peer review is under attack. Why continue to give their information (a key asset) to a commercial company, Publons,[150] who may not exist down the road (it was founded in 2012 and purchased by Clarivate in 2017)? Why not build a decentralized system and eliminate the middleman who now has a stake in the publishing process? That pitch was repeated at the September meeting in 2019, but in the end the publishers chose to stay with Publons. Arguments for continuing the project did not provide sufficient pressure to raise the project higher in the publishers' priorities in light of other factors which at that time had to be considered, such as: 1) the next step would require an investment, and publishers were concerned that Open Access, Plan S,[151] etc., might put a strain on their revenue stream; 2) the building of the infrastructure was in the hands of a small technology start-up (three people); 3) ultimately the project would need to find an organizational home or a non-profit organization would have to be established to oversee it; and 4) there was an existing alternative already being used by the publishers, Publons, which provided a system that can integrate seamlessly with a publisher's peer review submission system to streamline the process of recognizing their reviewers. Interestingly, the fact that blockchain was a new, young technology that requires trust, but had been proven to work was not a major issue. In summary, a system that worked (albeit not blockchain-based) already existed and Clarivate is not a competitor to primary publishers. The peer review project was terminated, but not because the technology did not work – it did. In further support of these observations about the appropriate application of blockchain technology Sean Manion said during his interview that blockchain technology, when applied to a specific use case, may not be needed for that use case, so when it "fails" one has to ask if the failure was due to the technology or to human concerns, e.g., will the implementation risk an organization's business model, is there a concern about sharing a platform with competitors, etc.? One must wonder in this specific case how much the last concern that Sean mentioned impacted the publishers' decision.

Van Rossum added that if the Bloxberg Consortium discussed in Section "Bloxberg Consortium" had existed when his initiative started, he would have gone to them for the technology piece. They would have been a great player to interact with the large publishers who were involved with the project, and it would have allowed the publishers to engage with the consortium members in a new way. He does not view the project as a failure, but rather as a useful experiment from which others can learn. More importantly, the critical lesson to be learned out of all of this is that blockchain can play a major role if you do not have a trusted middleman already providing the required service unless there are other compelling reasons – time and cost reduction, increased revenue, improved service to stakeholders, etc.

Clinical support tools

The second example of where blockchain technology ended up not being a good fit was when Elsevier was looking to use blockchain for one of their clinical support tools. We found out about this because they gave a presentation on this particular use case and why it failed, and it was brought to our attention when we interviewed Sean Manion. He graciously put us in contact with the person who gave the presentation, James R. Sacra, who was, at the time of their foray into blockchain technology, a senior director in Elsevier's Precision Medicine group within Clinical Solutions and he kindly agreed to be interviewed for this paper. In 2016 Elsevier bought a small company that had a clinical trial and design study product called "MACRO" – MACRO V4 to be specific, and at that time it was still very much in use, particularly in the UK.[152] His group was tasked to see if they could create a next-generation clinical study design and capture tool. Their goal was to find out how they could ensure the validity of data in a research process in the clinical space. Blockchain seemed to be a potential answer because it ensures that data cannot be overridden – an essential aspect of a clinical research study. So, they decided to learn more about the technology. One of the interesting aspects was trying to balance the real-time exchange of data and the process required to upload to a blockchain (e.g., waiting in a queue). They were concerned about how they could manage this in line with the user's expectation of their product. Another issue was the cost of moving data onto a blockchain. Elsevier is a commercial organization and wants to cost-effectively create products that people need and will buy. However, they decided not to let cost limit them in the beginning. The time issue was more problematic, so they thought that they might just use blockchain as an audit history of the data rather than for the real-time exchange of data. This did limit what they were leveraging blockchain to create, but on the other hand, the technology certainly worked to ensure the validity of the data and that was one of the main issues that they were attempting to address. So, they decided to take the audit history goal for the use of blockchain.

They then discovered that there was another requirement for the product that was popping up in their market research. Customers did not just want to use Elsevier's clinical trial tools for research design – they wanted to use them for clinical registry. Looking at this issue they ran into the laws around "the right to forget and the right to be forgotten"[153] which vary from country-to-country (see Section "Blockchain Technology: Legal & Regulatory Considerations" on legal and regulatory considerations). They then tried to see how they could handle this by separating the components of the tool (public vs. private) and finally came to the realization that they were having to design around blockchain rather than with it. The particular use case for which they were designing was not a good fit for the technology at that time. They needed technology that would add value and expedite bringing the product to market and blockchain was not working so they walked away from it. When we spoke to Sacra he still strongly believed in the value of the technology, but noted that it must be the right solution for the task at hand, for example some of the use cases we have described earlier such as document management, intellectual property, real estate transactions, etc.

Lessons learned

During the development of this white paper, we asked those whom we interviewed what lessons they learned during their blockchain journey and what relative strengths and weakness came from applying blockchain technology in the scientific process. Many offered the same words of wisdom which we repeat below. Heed their advice well.

- Blockchain will not solve every problem, so users need to understand what they are trying to accomplish.

- Data standardization is essential and where that does not exist blockchain usage could be problematic (this emphasizes the importance of IUPAC's efforts in developing data standards).
- Administrative use cases can really benefit from blockchain technology. They usually have good data standards and are the easiest and fastest applications to implement (although they may be considered boring, use of the technology can create greater efficiencies and cost savings for these use cases).
- When considering using blockchain technology in your organization or industry ask the question – is this the right technology for my specific use case? The use case must be important, but it probably should not be business critical, especially if you are going from proof-of-concept to minimal-viable-product to production. Take it step by step – break it down into manageable pieces.
- The use of blockchain technology comes with some overhead. It requires learning and it requires that you think differently so that you can see how it fits into what you are attempting to accomplish. It requires a champion and a willingness to extend the energy required to fully understand the technology and what it can do.
- For each step of the research work flow the following questions should be asked:
  1) Where can things be improved?
  2) Can blockchain/distributed ledger technology facilitate and/or incentivize? Note that incentivizing is for advanced use cases (see for example Sections "Molecule and Bloxberg Consortium") – don't start with it, get the infrastructure/scaffolding in place first as did the Bloxberg Consortium.
  3) What would be the cost/benefit and return on investment (ROI) for implementation of a blockchain technology solution? Answering this question can be challenging, especially when it may be difficult to put a value on the benefits of a blockchain-based solution, but as with any project implementation decision, it is important to attempt to do this up front.
  4) If the goal can be achieved without blockchain/distributed ledger technology, why has it not been reached? Is the pushback against the use of blockchain due to the technology or due to some human factor? Blockchain is not the solution for every problem, but where it can make a real difference, why is it being ignored?
- Scientists have no time, patience, or bandwidth to deal with an additional overlay on their workflow. Blockchain applications need to be seamless and embedded in the systems that researchers already are using.
- Blockchain use cases involving tokens or other forms of cryptocurrency that have inherent financial value will more than likely come under some form of regulation as will use cases that involve privacy issues, for example where the General Data Protection Regulation (GDPR)[154] weighs in. Know what you are getting into and do your research up-front (see Section "Blockchain Technology: Legal & Regulatory Considerations" on legal and regulatory considerations).
- Regulators need to be educated and informed and it comes down to how the institution using blockchain technology wants to proceed – are they restricted, or do they have a lot of freedom? The burden is on the platform developer to educate and to ensure that all the stakeholders around the development fully understand what they are creating, how it works (including governance), etc. This education extends to regulators who need to be informed as to how blockchain technology works in relation to the area(s) under the regulator's remit to adjudicate and decide. This is especially important when funding is involved and where privacy at the individual level needs to be protected.
- If any technology – not just blockchain – makes the lives, jobs, workflows, etc. of individuals and institutions easier they will investigate it, try to understand it, and adopt it. No matter how loud a community of enthusiasts shouts about the value of a technology, people must see it for themselves; they need to know that it is not too complex for them to use. The key is to demonstrate that the technology makes things easier, offers a smoother workflow, makes things more secure, is better than the existing solutions, and can be used with the click of a button. Researchers do not want additional work that could distract them from their primary goal.
- Academics and some large organizations can be slow to adapt to the ability of technologies to speed information sharing in ways that enhance impact, provide insights for evaluations, and increase the level of trust and reliability of research findings. So far it is the younger, early career researchers who have been willing to

experiment and use new services. Overall, the challenges to adoption of blockchain are more behavioral than they are technological, and winning adoption of this technology will come along as projects that make it easier to implement and use emerge.

Lessons learned from consortia

- Consortium usage of blockchain technology (i.e., a group of companies working together) is more effective than single-entity usage because the technology can automate the trust among the organizations that are collaborating, e.g., pharmaceutical companies, healthcare networks, etc., because they can share information without revealing everything (controlled sharing). However, consortium usage requires both technical development and governance as noted by the Bloxberg consortium. They said that 50 % of their work is technical development; the other 50 % is organizational – community maintenance, administrative, and legal. Governance can be challenging.
- One of the main challenges for consortia is getting consortium members to share the *de minimis* amount of information – what needs to be shared to get the kind of transparency and assurance that all parties involved need at the end? This challenge/hurdle exists for many enterprise-related blockchain use cases, whether in healthcare or in the conventional corporate world.
- The challenge for enterprise distributed ledger and blockchain implementations is getting that consortium of the willing to gather, to agree on the value of the benefits, and to start the journey of collaboration together. They need to decide, often at a fundamental operating level, what information needs to be shared and why? Who has access? Who is running the nodes? What data and information are they as a group going to rely upon? How does this integrate into their own internal systems, and how do they play with interoperability more generally to the extent there are other initiatives within their ecosystem to promote interoperability?

When we interviewed Dr. Naseem Naqvi, Editor-in-Chief for *the Journal of the British Blockchain Association*, he said that he believes in applying an evidence assessment framework when considering the potential use of blockchain technology[155] and tells people to take what he calls the "PICO" approach: P – what is the problem; I – what is the new intervention; C – how does it compare to the existing intervention; and O – what are the outcomes and the evidence that it is better and that it works?

His ideas are summarized in an approach that he terms Evidence-Based Blockchain and the comments in his article[156] on this approach echo the "lessons learned" noted in this section.

Naseem himself is very enthusiastic and passionate about the technology, but made it clear that there are practical implications, regulatory issues, and many other things that inhibit a successful application. He views that the technology's major contribution is providing a data audit trail with immutable timestamps and noted that in scientific research the practical implementation of blockchain is targeted at protecting intellectual property – pre-published data, articles, etc. as well as for published work. Dr. Naqvi said that blockchain could certainly be applied to research funding because it allows for the transparent allocation of funds, the auditing of spending, and the tracking of funds. But how this would play out with regards to regulatory and policy issues remains to be seen. He noted that regulations and policies are very important and this needs to be highlighted in the white paper – which is the perfect segue into the following section – Blockchain Technology: Legal & Regulatory Considerations.

Blockchain technology: Legal & Regulatory Considerations

While this paper is focused on highlighting where blockchain technology could be used most productively in the scientific workflow, it is important to provide some broader insight and information on the wider legal and regulatory (L&R) aspects of blockchain and distributed ledger technology (DLT) so that you can understand why some projects may not have worked out as envisioned. When we defined the steps along the scientific research workflow at the beginning of Section “Blockchain Applications Along the Scientific Research Workflow”, we said that it matched the workflow described by Sean Manion with one exception – his workflow included a step for obtaining regulatory approval, an essential step in the healthcare, pharmaceutical, and financial sectors among others, and a hurdle which his health-related blockchain-based activities must overcome. While L&R aspects do not impact all blockchain-related businesses, they are a critical part of the blockchain ecosystem which one must consider. Consequently, this section aims to provide some broader insight and information on these wider L&R aspects. It is *not* aimed at guiding individuals or companies who want to set up or run blockchain-based businesses, and it should be stressed that the purpose of these few paragraphs is not to provide definitive legal guidance and advice. Not one of the authors of this paper is a lawyer! We simply want to highlight some of the issues of which you should be aware.

What this section will endeavor to cover is some background on legislation and regulation as it currently applies to blockchain technology for organizations who want to “use” the technology. Furthermore, to avoid confusion in this section the terms “legal,” “legislation,” and “regulatory/regulation” will be used somewhat synonymously. This is admittedly incorrect; legislation is law passed by a legislative body, while regulation is a set of rules or guidelines issued by an executive body such as a government agency or regulatory board in compliance with the law.[157] However, for the sake of simplicity, we will cover both the legal and regulatory considerations of blockchain technology together. Another reason for covering them as one topic is that the area of blockchain and distributed ledger technology is still rather immature and rapidly evolving. As a technology it is impacting and disrupting multiple businesses and industries, both regulated and non-regulated. Consequently, governments and legislatures across the globe are still trying to “get their heads around” what laws and regulations might be needed to help blockchain become a “safe” technology for the people and businesses in their individual jurisdictions, to protect customers and prevent criminal activity. For example, in countries such as the United States, the L&R aspects of blockchain technology are made even more complicated by the federal nature of the U.S. government where both central national government AND local, regional (state-based) governments can generate their own, sometimes even conflicting laws and regulations.[158,159] An example of this occurred in 2018 when the U.S. state of Wyoming enacted several blockchain-enabling laws which, at the time, made it the only U.S. state to provide a comprehensive legal framework to enable blockchain technology to flourish, both for individuals and companies. On the other hand, in 2014 New York state put in place legislation around cryptocurrencies in the form of its BitLicence.[160] At the national level in the U.S. in 2019–2020 32 bills covering blockchain and cryptocurrency were introduced to Congress: 12 bills addressing the use of cryptocurrency in potential terrorism, money laundering, human, and sex trafficking; 13 bills focusing on the regulatory framework and treatment of cryptocurrency and blockchain; five bills promoting ways blockchain technology could be used by the U.S. Government; and the two more recent bills covering the concept of a digital dollar.[161] Similarly, in 2021, the 117th Congress introduced 35 bills,[162] perhaps the most relevant to this paper being: (i) the Blockchain Technology Coordination Act of 2021 (H.R.3543)[163] which at the time looked to establish “a National Blockchain Technology Coordination Office within the Department of Commerce;” (ii) the Blockchain Innovation Act (H.R.3639)[164] which required “the Department of Commerce to consult with the Federal Trade Commission and other relevant agencies to study potential applications of blockchain technology (i.e., the technology that supports digital currencies such as Bitcoin), including the use of such technology to address fraud and other unfair or deceptive practices;” and (iii) the Blockchain Promotion Act of 2021 (S.1869)[165] which directed the Department of Commerce “to establish the Blockchain Working Group to submit a report to Congress which contains a recommended definition of the distributed ledger technology commonly referred to as blockchain technology, and other specified recommendations regarding this technology.” Although these three bills were introduced to Congress in May 2021, none of them, unfortunately, received a vote and none was enacted. Nevertheless, it demonstrates the importance that the U.S. government puts on blockchain technology and the need to consider its impact and ramification further, so much so that bills continue to be put to the 118th Congress on blockchain and crypto assets (e.g., H.R. 1747 and H.R. 1460) to name but two.[166,167]

It is important to note that a great deal of blockchain law and regulation has been focused on the financial industries (also known as Fintech[168]). This prioritization of Fintech was driven by the original blockchain use-case of bitcoin and cryptocurrencies, as well as some early scandals around cryptocurrency exchanges such as Mount Gox.[1,169] At the time of this writing there remains a great deal of activity and attention globally on the L&R aspects of Fintech and "decentralized finance" (DeFi).[170,171] This is especially true in the U.S., where the areas of Initial Coin Offerings (ICOs),[172] stablecoins,[173] and non-fungible tokens (NFTs)[59] have come under a great deal of scrutiny. This has particularly been the case around cryptoassets and cryptotokens, and whether these are "securities" as defined by the Howey Test.[174] However, in view of the more scientific focus and scope of this paper, we will not go into these complex and still somewhat unclear areas in any more detail, except to say that artefacts such as NFTs are attracting some interest in the broader scientific community in use-case areas such as fundraising and monetizing personal data (e.g., genomic data).[175]

Laws and regulations applicable to industries such as Pharmaceuticals and Chemicals have on the other hand, been slower to develop. In this section, rather than go into comprehensive detail about specific laws and regulations and their effect on the use of blockchain technology, we briefly describe four general use-case examples, which we believe will give a suitable introduction to the L&R issues associated with blockchain technology. We include several links and references to freely-available online articles and sources of information for readers to explore further. As always though, if you want to know more detail, especially within your geographic region, please seek more professional legal advice.

Blockchain technology and privacy: the general data protection regulation

It is a widely held belief that transactions performed on a blockchain are anonymous and hence private. On public blockchains, this belief is incorrect.[176] Transactions on public blockchains such as the bitcoin blockchain are "pseudonymous" meaning that your actual identity is hidden behind one or more hexadecimal strings (your private and public keys).[177,178] Whilst it is possible to obfuscate your identity on a blockchain using more sophisticated techniques such as zero-knowledge proofs[179] and transaction-joining protocols,[180] it is always worth remembering that it is possible, albeit not easy, to identify who performed a transaction on a public blockchain. Misunderstanding of the connection between blockchain technology and anonymity, and hence privacy, has led to many concerns about the use of blockchain technology to transact and manage private data. This has been particularly true in the European Union (EU) because of the General Data Protection Regulation, or GDPR.[154]

GDPR is a legal framework which sets guidelines for the collecting and processing of personal information from individuals who live in the EU. Since the regulation applies regardless of where websites or systems which might collect personal information are based, it must be heeded by *all* sites that attract European visitors, even if they do not specifically market goods or services to EU residents.[181] A key aspect of GDPR which directly conflicts with the foundations of blockchain technology is the legal right to be "forgotten" – in other words your legal right for any information about "you" on any system stored by an organization anywhere in the world to be deleted at your request. A prime tenet of blockchain is its immutability and the absolute inability to edit, let alone delete data or metadata[182] held in one or more of its blocks. This tension has led many organizations to avoid using certain blockchain technologies when seeking to manage personal data (e.g., clinical trial data). However, judicious choice of the right DLT can make the benefits of blockchain accessible, even for personal data. More specifically, the use of private or more tightly controlled, permissioned blockchains can circumvent this apparent barrier, even in Europe.[121,124] For more information on blockchain and the GDPR please refer to a recent report on this topic.[183]

1 It is important to realize that the recent FTX bankruptcy alluded to elsewhere in this paper[7] was not the first highly hyped cryptocurrency failure. Mount Gox took place in 2014, but it did not deter the use of blockchain technology outside of the financial arena.

Blockchain technology and intellectual property

One use case area that would seem to be a good "fit" for blockchain technology[184] is that of intellectual property protection. Blockchain provides the ability to capture a time-stamped, immutable record of an original innovation, most easily through a unique cryptographic hash of a document. As noted in Sections "Blockchain Technology: What is it? and Blockchain Technology: A Brief History" in this paper, so-called "hashing" of data is a critical component of blockchain technology. In summary, hashing is the process of putting a computer file of any kind (document, image, sound or video file, etc.) through an algorithm which compresses the entire file, including not just its content, but also its formatting, into a defined multi-character hash string.[185] For every file, that hash is unique and exactly represents the content and format of the original file.[186] Putting a hash of an original document onto a blockchain achieves two things:

1) It provides an immutable record, in a small piece of text (the hash string), of the existence and the content (albeit cryptographically concealed) of a file.
2) It provides a confirmed timestamp for when that hash was installed on a blockchain.

With these two properties, anyone who has a file which, when hashed using the right hashing algorithm, generates a hash which is identical to one already present in a block on a blockchain, knows that the file that they have is identical to a file and its content which existed at the time the original was mined into the particular blockchain. By this mechanism the blockchain operates as a surrogate file and document registry.

Storing hashes of original documents or files on a blockchain is an obvious potential for the use of DLT in the protection of intellectual property in all its forms, of which evidence of creatorship is only one, but it has yet to be fully explored legally.[187] Nevertheless, various governmental agencies and IP registries such as the European Union Intellectual Property Office (EUIPO) are actively looking into the capabilities of blockchain. Relatively recently the U.S. Congress created a Congressional Blockchain Caucus as a platform for industry and government to come together to study and understand the implications of blockchain technology.[188–190] One other key point to note in this "blockchain & IP" section is another extensive strand of L&R discussion and publication which covers how to generate IP on the topic of blockchain technology – i.e., where the foundation of the IP is "the blockchain" itself. This area does not fall within the scope of this paper so is not covered in any more detail here, but for more information on this often-complex topic please refer to this report.[191]

Blockchain technology and supply chains: the FDA pilot

One of the most important global regulatory bodies is the U.S. Federal Drug Administration – the FDA. The FDA's primary responsibility is to "protect the public health by assuring that foods (except for meat from livestock, poultry and some egg products which are regulated by the U.S. Department of Agriculture) are safe, wholesome, sanitary, and properly labeled; ensuring that human and veterinary drugs, and vaccines and other biological products and medical devices intended for human use are safe and effective".[192] The FDA's position on blockchain technology was mentioned in the agency's 2019 Technology Modernization Action Plan (TMAP).[193] In that plan, it was stated that "Data-informed technologies, such as distributed ledger solutions such as blockchain, will be essential to support the FDA's track-and-trace priorities." Consequently, the FDA then announced[194] the launch of a pilot program under the Drug Supply Chain Security Act (DSCSA) in which "participants representing the drug supply chain can pilot the use of innovative and emerging approaches for enhanced tracing and verification of prescription drugs in the U.S. to ensure suspect and illegitimate products do not enter the supply chain." This led to four organizations, IBM, KPMG, Merck, and Walmart, to propose a pilot program to examine the use of blockchain technology in verifying and tracking pharmaceutical products in preparation for future DSCSA requirements. The two objectives of the program were to:

1) Demonstrate that blockchain can provide a common record of product movement by connecting disparate systems and organizations to meet DSCSA 2023 interoperability requirements in a secure way.

3) Improve patient safety by triggering product alerts and increasing visibility to relevant supply chain partners in the event of a product investigation or recall.

The results of the pilot were reported in 2020[195] and the four component organizations agreed that not only was the program a success, but also that "there are benefits to using blockchain both for, and beyond, DSCSA compliance."

The use of blockchain technology to support and enhance the management of supply chains in multiple industries, from food to luxury goods, and logistics more widely has, outside Fintech, been one of the technology's primary use-cases and this seems likely to be a major area for DLT in the years to come.[196,197]

Blockchain technology and GxP: enabling adherence to regulations

The blockchain-FDA example above describes how blockchain technology has the potential to help organizations better comply with specific legislation. Blockchain technology also has the potential to enable better and more effective adherence to regulations. The regulatory use-case example we will briefly describe is the potential for blockchain technology to help with good working and operating practices in the domain usually referred to as "GxP".[198] The 'x' in GxP is a catch-all abbreviation to cover the variety of different good practice regulations that exist. Well-known examples include Good Laboratory Practice (GLP); Good Manufacturing Practice (GMP); Good Clinical Practice (GCP). More specifically, GxP is a set of good practice quality guidelines and regulations, employed around the world in regulated industries such as pharmaceuticals, food, medical devices, and cosmetics. GxP has been put in place to ensure that the products and services from these industries are safe and meet their intended use. There are several essential components which enable GxP compliance. These are: (i) the People; (ii) the Processes; (iii) the Kit, Devices, and Facilities; and (iv) the Inputs and Outputs. In all four of these areas blockchain technology could be of significant assistance to help with compliance,[199] but to pick just two (for brevity): in the "people" area, blockchain technology could help provide better personal digital identity, which is itself another important potential use-case for blockchain technology,[200] and/or to better manage training records and qualifications[136] as noted earlier; these could enable better Good Laboratory Practice (GLP) compliance. Secondly, in the kit, devices and facilities area, as noted in Section "Medical Device Tracking" of this paper, blockchain technology is already being used to track and manage the maintenance of medical devices and equipment, but that use could be extended to cover bigger equipment and facilities in manufacturing and therefore help with better Good Clinical Practice (GCP) and Good Manufacturing Practice (GMP) compliance.

Blockchain legal & regulatory considerations around the world

In this section, we have focused mainly, but not exclusively, on the L&R considerations and issues as they apply to the United States at both the national government and state levels. The primary reasons for this are that we do not have the space in this paper to provide a comprehensive global view and, most countries (including the U.S.) are still in the process of developing and evolving their own sets of laws and regulations around blockchain technology. That situation is likely to persist for some years to come. However, we would like to provide you with some more links to reports and articles which describe in more detail how blockchain technology is being considered and, in some cases, legislated, in various jurisdictions around the world. All have been published since 2019.

- "Blockchain and the Law" – International and European perspective[201]
- "Blockchain and the Law: Regulations Around the World"[202]
- "Blockchain and the Law" – U.S.-focused [203]
- "How Blockchain Projects Can Succeed (and Avoid Legal Hassles) in the USA"[204]
- "Blockchain Regulation and Governance in Europe"[205]
- "Legal And Regulatory Framework for Blockchain" – EU-focused[206]
- "Blockchain: Legal and Regulatory Guidance Report" – UK-focused[207]

- "Blockchain and Cryptocurrency Regulations": Japan[208]
- "Blockchain and Cryptocurrency Regulations": Canada[209]
- "What the New PRC Blockchain Regulations Mean" – China-focus[210]

In closing, in this section we have endeavored to provide a very brief introduction, through four broad use-cases, to the legal and regulatory challenges of using blockchain and distributed ledger technology from the primary perspective of how these new technologies are impacting the scientific industries. For the sake of brevity, there are several areas we have chosen not to cover, e.g., blockchain governance; some of those we have omitted are outlined in a separate article.[211] We have also provided links to reports with a broader coverage of the legal and regulatory aspects of blockchain technology and we urge the reader to refer to these if they want to know more about this complex and still-evolving area. One more recent regulatory framework that does warrant further mention is MiCA, the European Union (EU) regulatory framework designed to establish uniform market rules for crypto-assets across the EU. MiCA aims to protect investors, innovators and collaborators, and promote the widespread adoption of blockchain and distributed ledger technology (DLT) in the EU's virtual asset sector by providing legal certainty. More importantly, MiCA provides a firm legal basis for the incentivization, and the possible monetizing of scientific assets in the EU.[212]

Finally, while it may appear that the areas of blockchain and DLT are complex, daunting, and subject to a great deal of uncertainty regarding regulations and the law, what is certain is that this technology will impact and disrupt the science-based industries in the coming years. How it will disrupt and how visible that disruption will be, is yet to be seen, but we do believe that blockchain and crypto technology will come into scientific businesses in unexpected, but productive ways. Scientists should be prepared for that disruption, and they should, in our opinion, embrace it.

The present and future of blockchain technology: technical capabilities and challenges

When we began the journey to develop this white paper, a relatively short time had passed since the creation of blockchain technology. Despite this, the discipline, which is located at the crossroads of cryptography, computer networks, and the digital economy, has already evolved over three distinct generations (Fig. 4). The purpose of this section of our paper is to delineate those generations, demonstrate the incredible growth of blockchain's capabilities, and indicate the challenges that lie ahead. Also, at the outset, it is essential to note that the new generations do not replace the older ones, but rather, they build upon them.

The first generation

As we stated earlier, the first generation of blockchain, exemplified by Bitcoin and based upon the 1991 work of Haber and Stornetta, was born in 2008.[27] It was based on a conceptually simple consensus mechanism, proof-of-work. From the application/use case perspective, the technology was designed simply to form the technological base for a new kind of electronic money, cryptocurrency, by providing mechanisms to prevent double spending. While some exciting applications existed outside the domain of cryptocurrencies, such as Namecoin[213] which was intended to change the way the Domain Name System (DNS)[214] worked, the first-generation blockchains did not offer mechanisms that would enable a dynamic growth of new applications.

In terms of design, the technology was introduced by the relatively high-level white paper, Nakamoto's "Bitcoin: a peer-to-peer electronic cash system,"[27] and the open-source computer code. There was no authoritative, detailed specification separate from the code. While this approach worked quite well initially, it was an obstacle on the path toward applications beyond cryptocurrency.

Even so, the most popular and iconic first-generation blockchain, Bitcoin, still dominates the cryptocurrency market. Notably, at the time of writing, two other first-generation blockchains, Dogecoin[215] and Litecoin,[216] still top the chart of the most popular cryptocurrencies.

The second generation

One of the most distinctive aspects of the second-generation blockchains is the capability of offering functionalities that exceed those needed by crypto-assets systems. The most important feature is the systems' capacity to execute smart contracts, in other words, pieces of software that can represent transactions or events in both the real and digital worlds, and which are also relevant within the context of business relations between the parties to a contract. Properties such as these allowed the second-generation blockchains to offer platforms for carrying out legally-binding actions with no central intermediaries. As regards the security features developed in the era of the first-generation blockchains, their second-generation counterparts lowered arbitration costs and significantly reduced the risks of fraud and technical failures in the digital infrastructure used for the transactions.

The most significant blockchain of the second generation is Ethereum which was first mentioned in Section "Blockchain Technology: What is it?", and which is also a crypto-asset platform. However, its fundamental attribute is the availability of a Turing-complete programming platform. The Turing-completeness[217] of a platform allows it to act as a computationally universal environment, enabling every possible computer algorithm to be executed. As of this writing, the Ethereum coin, known as Ether (ETH), is currently the second most valued crypto asset after the first generation's Bitcoin.

Thanks to its radically new features, Ethereum brought multiple 'derivative' tools into play. The most noteworthy are the ERC20[218] token used for an Initial Coin Offering (ICO),[219] a crypto economy analog of the Initial Public Offering (IPO)[220] for real-world businesses, and the Non-Fungible Token (NFTs), which are used for the creation of unique digital objects. NFTs, as mentioned earlier (e.g. in Sections "Matryx and Blockchain Technology: Legal & Regulatory Considerations") can be used to represent ownership of nearly any object, tangible and intangible alike, which can be expressed in digital form.[221]

When it comes to design, Ethereum introduced something known as 'client code,' a new way of creating alternative software solutions compatible with the original at the protocol level rather than the source code compatibility level. The availability of detailed specifications has created several alternatives; in other words, it has facilitated many and varied implementations using a range of programming languages. All these systems can work together on the same network without problems.

Second-generation projects also offered a variety of different consensus mechanisms. As we have previously indicated in Section "Blockchain Technology: A Brief History" this paper, Ethereum was rolling out proof-of-stake consensus mechanisms with the final act of that process (called "The Merge") played out on September 15th, 2022.[222] However, other consensus mechanisms or "protocols" such as delegated proof-of-stake (DPoS),[223] proof-of-burn (PoB),[224] practical Byzantine fault tolerance (pBFT),[225,226] and many more gave the second-generation blockchains a much higher transaction throughput, while reducing the associated energy consumption.

There are a great many interesting second-generation projects. It is worth mentioning the NEO blockchain,[227] which created an ecosystem intended to become the foundation for the next generation of the internet by providing tools for digitized payments, digital identity, and digital assets of a general kind. NEO has also proposed a unique consensus protocol. Known as delegated Byzantine Fault Tolerance (dBFT),[227] it represents an improvement on the pBFT protocol and has enabled NEO to exceed the 1,000 transactions-per-second (TPS) limit. By way of comparison, the credit card organization Visa can process over 1,700 transactions-per-second.[228]

Another noteworthy case is the ICON project,[229] which is sometimes regarded as a precursor to the third generation of blockchains, given that it is focused on interoperability. It implements a 'blockchain transmission protocol,' enabling independent blockchains such as Bitcoin and Ethereum to exchange transactions. ICON adopts the Byzantine Fault Tolerant Delegated Proof-of-Stake (BFT-DPoS) consensus protocol[11] and the economic-governance Delegated Proof-of-Contribution (DPoC) protocol.[230]

The Hyperledger community mentioned in Section "Blockchain Technology: A Brief History" mostly contains second-generation blockchain projects. However, the recent release of Hyperledger Fabric (version 2.2 LTS)[231] is also a big step toward third generation blockchains.

The third generation

In spite of the successes achieved with the second-generation blockchains as regards both the quality of their use cases and the technological innovations that they proposed, numerous unresolved major challenges remained, primarily related to scalability (the number of transaction per unit of time and/or number of network nodes), interoperability (the ability to work in an ecosystem where other blockchains exist), the protection of user and data privacy and confidentiality, and essential data management, particularly on-chain data management.

Some analysts saw the arrival of Decentralized Applications (DApps) on the second-generation blockchain scene as the birth of the third generation of blockchains.[232] DApps enabled the blockchain industry to have a real-world/business purpose. Blockchains of the third generation directly addressed the challenges of scalability, privacy, and interoperability which were identified as issues of concern in the previous generations.

Directed acyclic graph-based distributed ledger technologies

The quest for much higher scalability lay behind the development of solutions based on Directed Acyclic Graphs (DAGs).[233,234] An alternative or even, perhaps, a rival to blockchain, DAGs are types of Distributed Ledger Technology (DLT) solutions. A DAG DLT[235] is a network of individual transactions linked to other transactions. DAG-based networks do not have the linked lists of blocks that the classic blockchains do. In structure, they resemble a tree formed by branching transactions. The use of DAGs and the elimination of costly replication and consensus over blocks of data means that these solutions offer the theoretical throughput of millions of transactions per second (TPS) without the need for expensive mining. In practice, existing DAG-based DLTs reach a throughput of 10k TPS.

Notable examples here include IOTA,[236] which was designed for large-scale internet of things (IoT) networks. However, with its design of consensus protocol, Fast Probabilistic Consensus (FPC),[237] it has become a regular cryptocurrency platform.

Another important DLT technology that uses DAGs is Hashgraph,[238] with its patented 'gossip about gossip' protocol for building directed acyclic graphs of transactions. In effect, the protocol resulted in the creation of a special kind of asynchronous Byzantine Fault-Tolerant (aBFT) consensus algorithm. However, unlike the classical

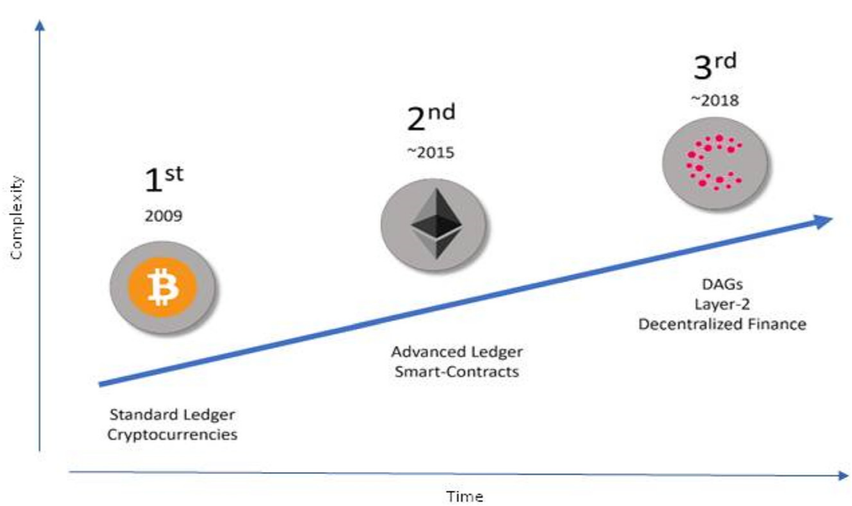

Fig. 4: The three generations of blockchain.

blockchains, Hashgraph transactions are not stored in blocks. Instead, strictly enforced transaction time-sequencing creates a secure, high-speed distributed ledger in the form of a DAG. Unlike most DLTs, Hashgraph is not open-source, and the only network running the protocol is Hadera Hashgraph.[239] Its cryptocurrency is HBAR.[240]

However, despite the high transaction throughput, there is still no wide-ranging industry consensus on how much trust can be placed in DAG-based DLTs. Both IOTA and Hashgraph, as well as other DAG DLTs such as Nano[241] or Obyte[242] (formerly Byteball), have drawn a considerable amount of criticism concerning the uncertainty as to whether they provide enough security, even against fundamental threats such as double-spending attacks.

Multilayered blockchains

The uncertainties surrounding DAG-based DLTs, and the innovations of developers associated with traditional, first- and second-generation blockchains have given rise to solutions that have expanded the capacities of the second generation of blockchains, rather than replacing them. There are a great many interesting proposals for such expansions, however the most important are those related to multilayered architecture.

The multilayered nature of blockchain architecture brings a clear separation of the software responsible for transactions from the software accountable for maintaining the entire network and smart contracts. The underlying reason for this is that it increases the network's capacity and speed. One of the most prominent examples of multilayered blockchains is Cardano,[243] with ADA,[244] its cryptocurrency, numbering among the highest valued of those related to third generation blockchains.

Nonetheless, an entire family of innovative third generation blockchain solutions known under the umbrella term of 'Layer-2 solutions'[245] contains the most noteworthy examples. These new systems are built on top of the second-generation blockchains, which are classified as Layer-1 solutions. In general, the Layer-2 systems achieve a much higher level of efficiency by limiting the dissemination of every transaction to the whole network. This is achieved by executing them in a separate part of it, known as the off-chain mode. The use of the main chain, which is usually expensive and slow, is then only used when needed to resolve potential disputes. Layer-2 off-chain operations are performed in sidechains pegged to the main chain. The Layer-2 architecture is illustrated in Fig. 5.

While the 'Lightning Network', which was invented back in 2015[246] and built on top of Bitcoin, was the first Layer-2 solution implemented in practice, most of the innovative ideas originated in Ethereum developer circles. The first such idea was Plasma,[247] which can be visualized as a living tree[248] with numerous branches, rather than as a linear chain. The main blockchain is then depicted as a trunk. In most cases, Ethereum, which is supported by its trusted consensus mechanism, guarantees security and the flow of proofs, much like a trunk supplying energy and nutrients to its branches. And in another analogy, the main blockchain plays the role of a Supreme Court, which imparts judicial powers to the lower courts. The two most important Layer-2 networks today are Polkadot[39] and Polygon.[249]

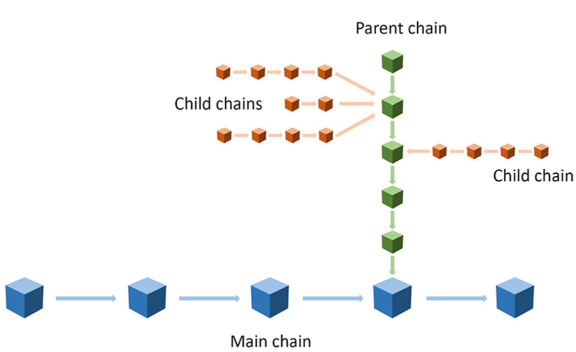

Fig. 5: The conceptual architecture of Layer-2, third-generation blockchains.

Layer-2 solutions form the technological basis for the recent rapid growth of blockchain-based financial instruments previously offered only by centralized institutions such as banks, stock exchanges or organized stockbrokers. These instruments include lending and borrowing, trading derivatives, providing insurance against transactional risks, and earning interest on the crypto assets working in an analogy to standard saving accounts. They are also known generically as 'Decentralized Finance' (DeFi) and they, too, were made possible by the rise of DApps, and the transaction speed offered by Layer-2 solutions.

Interoperability-oriented solutions

In addition to scalability, third generation blockchains attempted to resolve other complicated problems relating to second-generation blockchains. Those problems can be identified as interoperability between different blockchain networks, privacy protection, and data management.

The two most important solutions with goals directly related to interoperability issues are Cosmos[250] and NeoX.[251] Cosmos blockchain architecture assumes the existence of several independent networks referred to as Zones, which are connected to the Hub, as the central blockchain is known. The separate blockchain Zones are then plugged into an ecosystem called the Cosmos Network.

NeoX also implements cross-chain interoperability by allowing its participants to exchange transactions between different chains in a fully transactional mode; in other words, the entire multi-chain transaction either succeeds or it fails completely.

The Polkadot Layer-2 blockchain mentioned Section "Multilayered Blockchains" also has interoperability high on its list of goals. "Related to Polkadot is another interesting third-generation project: Kusama".[252] Called by its creators a "canary network",[253] mostly for its experimental character and test-bed like applications, the Kusama Network introduced the concept of "parachains". A parachain is "an application-specific data structure that is globally coherent and verifiable".[254] As such, it usually takes the form of a layer-1 blockchain, but it can take other forms providing trusted computation. Kusama allows for the creation of an ecosystem with many different parachains, providing full interoperability with new and existing blockchains, such as Ethereum.

Privacy-focused projects

Privacy is another complicated blockchain technology problem. Traditional blockchain networks expose all their transactions and are completely transparent, meaning that their participants can be identified indirectly, at the very least, and tracked. Of course, there is a fundamental trade-off between protecting privacy as a fundamental value and protecting against cybercrime, including confidence tricks, internet fraud, and ransomware. However, some aspects of privacy can be addressed by the application of the pair-wise decentralized identifiers, Verifiable Claims, which are part of Self-Sovereign Identity (SSI)[255] solutions, and zero-knowledge proofs (ZKPs),[256] all of which are implementable as blockchain-based solutions. Some prominent examples in that domain are CoinJoin,[180] a privacy protection technology used by Dash[257] (a fork from Bitcoin), Monero[258] (using advanced ring signature technology), and Zcash,[259] which uses ZKPs.[256] A ZKP is a cryptographic technique by which one side can prove the truth of a fact to a second side without disclosing the details of that fact.

As regards SSI solutions, one of the most prominent blockchains is offered by the Sovrin Foundation[260] and its global digital identity network, which is based on the Hyperledger Indy framework. The standardization and advocacy group in that domain is the Decentralized Identity Foundation.[255]

Data management on blockchains

Finally, some third generation blockchains focused on data management. In a nutshell, they tried to offer a solution to another complicated problem, namely, data storage on a blockchain. For some applications of the technology, it is highly desirable to be able to store a significant amount of data using the on-chain mode. It is also desirable to store 'structured' data instead of the binary 'blobs' of the first-generation blockchains or the string-serialized data structures of the second generation.

A prominent example of this kind of solution is BigchainDB[261] from MongoDB, the authors of the popular key-value database of the same name. BigchainDB offers on-chain structured data storage with all the attributes of blockchains, in other words, data integrity, confirmability, non-repudiation, and high availability. Other companies pursuing on-chain data storage solutions include Storj,[262] Swarm,[263] Sia,[264] FlureeDB,[265] and Graph-Chain;[266,267] these are similar solutions based on modern semantic graph databases.

The future of blockchain technology: is the fourth generation coming?

In the light of the current development of the third generation blockchains, it seems somewhat speculative to write about the next generation, particularly when the real and long-lasting benefits of today's solutions still lie ahead of us. Nonetheless, this does not stop numerous authors from forging a vision of a future fourth generation, where all the previous challenges will finally be resolved and "trust in easy-to-consume ways"[268] will be enabled, "accelerating the formation, operation, and reconfiguration of business networks".[268] From the technology perspective, there are predictions about the vital role of Artificial Intelligence in the fourth generation blockchains.[269–271] There are new initiatives that have already been dubbed "fourth generation" blockchains. One of the more interesting is Multiversum,[272] which claims to "achieve syntony between IT security and cryptocurrencies universes".[273] Hydrus7, which is "built with robust advancements in a more structured and scalable manner with the help of AI, ML, Data Compression in Blocks, sharding,[274] and many other cutting-edge technologies",[275] is another. There are initiatives based on the concept of meta-tokens. For example, MetaMUI[276] defines meta-token as a "collateralized asset-backed metamorphic digital asset that can change the shape based on usage." Assuming these ideas materialize, we should indeed soon see the onset of fourth generation blockchains. However, it is still hard to judge whether we are indeed witnessing the birth of the fourth generation blockchains or if we are only seeing clever marketing narratives at work. Despite these uncertainties, there is an extremely interesting development of blockchain-related technologies, which could lead to a much stronger and more resilient ecosystem of distributed computing. It is worth mentioning technologies such as MPC (Multi-Party Computation), which is based on the most advanced cryptographic algorithms, and which allows for the deployment of secure privacy-preserving solutions. MPC[277] technology is a base for the most advanced custody solutions, which help people and organizations to manage their private keys in the most secure way and which may have application to other cases described in this white paper.

The impact of quantum computing

There is little doubt that another important, incoming information technology revolution will assuredly accelerate the development of blockchain technology. This revolution will happen because of the rise of practical quantum computing and quantum information technologies.

Until recently, quantum computing technology (QCT) was relatively unknown to the public. It has now become a topic of current popular interest because of the potential capability of quantum computers to deliver an unprecedented increase in computational power. Work on the hardware, software, and algorithms for this new reality of computing is now proceeding at full speed in academic and commercial environments. For obvious reasons, we cannot provide an overview of those efforts here. We can, however, refer readers to an excellent publication from the National Academies Press (NAP), Quantum Computing. Progress and Prospects.[278] The primary purpose in devoting some space in this paper to QCT is because of its potential threat to the one of the foundations of blockchain technology, cryptography and cryptographic standards and algorithms.

One of the most remarkable features of quantum computing is that the first, most essential algorithms invented for that domain were related to cryptography. More precisely, they could be classified as crypto analytical algorithms as their application for breaking or weakening most existing modern cryptographic algorithms was straightforward. Shor's algorithm[279] guarantees polynomial time integer factorization, making it possible to break existing asymmetric ciphers in a reasonable time. Grover's algorithm, known as the quantum search algorithm or function inversion algorithm, can weaken both symmetric ciphers and some hashing algorithms. In short, the rise of quantum computing could bring an existential risk to existing cryptography. This risk is recognized and adequately addressed by organizations responsible for the security of ciphers. The U.S. National Institute of Standards and Technology issued a clear warning in 2016.[280] Soon after, it initiated a standardization process for what is known as post-quantum cryptography.[281] This branch of cryptography is also known as quantum safe. It is defined as a set of rules and classic, non-quantum, cryptographic algorithms are assumed to be secure against cryptanalytic attacks by quantum computing algorithms.

Alongside quantum-safe classic cryptography, there has been enormous progress in the complementary field known as quantum cryptography, a branch of cryptography that uses quantum mechanical properties of matter to create cryptographic protocols.[282] The best-known protocol of quantum cryptography is Quantum Key Distribution (QKD).[283] It allows for the provably secure sharing of secret keys that can be used to encrypt and decrypt messages. There are ongoing debates as to whether the QKD protocol can provide the proper protection from possible attacks and if post-quantum cryptography is the right choice.[284]

The risks posed by quantum computing will also impact the further development of blockchain technology significantly. Cryptography, and asymmetric cryptography in particular, forms the foundation upon which blockchains are built. Quantum computing introduces a substantial threat by making asymmetric algorithms vulnerable to attacks, which could potentially lead to the discovery of users' private keys, thus posing an existential risk to the stability of blockchains. Furthermore, since this form of cryptography is crucial for secure communication between blockchain nodes, their integrity is also at risk.

There is plenty of literature which both addresses the dangers and indicates possible solutions.[285–287] However, despite some isolated attempts, until recently blockchain developers' communities are showing no significant interest in redefining the way new systems are built to deliver quantum resistance.

Quantum information technologies, along with post-quantum algorithms endorsed by NIST, have the potential to not only increase the security of blockchain systems but also to help them overcome the limitations that are common to blockchains and other distributed systems. This topic, among others, is detailed by Imran Bashir in a dedicated chapter titled "Quantum Consensus" in his book "Blockchain Consensus."[288]

When it comes to blockchain security, the earliest and most serious attempt was delivered by a team behind The Quantum Resistant Ledger (QRL) project.[289] The QRL has developed, and now runs, a blockchain system which uses post-quantum algorithms to ensure its quantum safety. David Chaum, widely recognized as the person who invented digital cash, runs an innovative blockchain platform called XX network,[290] which claims to be quantum safe. XX network uses post-quantum cryptography to achieve quantum safety. Another project declaring quantum-safe operations using post-quantum crypto is the QAN Platform.[291]

Quantum Blockchains,[291,292] a startup launched in 2020, is building the foundations for the future of blockchains using quantum cryptography.[293] The project recently introduced what the company calls QSB – Quantum Secured Blockchain, built on the three pillars of quantum-resistant cryptography: Quantum Key Distribution (QKD), Post-Quantum Cryptography (PQC), and Quantum Random Number Generation (QRNG). Their white paper, which describes the implementation, has recently been made available.[294]

Closing comments on blockchain development

In closing this section on the status and future development of blockchain technology, it should be clear that the pace of invention has been rapid and that three distinct generations of blockchain technology can already be identified – all this despite the short history of running blockchain platforms. Each generation has been technically more advanced than its predecessor and has allowed for qualitatively different applications, from the cryptocurrencies of the first generation, through the smart contracts of the second, to the third, where we arrived at decentralized finance and a variety of other applications.

We are now creating an entirely new digital assets economy and a multiplicity of applications for use cases going beyond the crypto economy. The direction in which technology is advancing is opening new opportunities for "non-cryptocurrency" cases. For example, applying the layer-2 paradigm means that it is now acceptable to launch brand new child chains 'pegged' to the main net of a respected network such as Ethereum. A child chain of this kind can be designed for special applications such as digital credentials, attribution, supply chain and the internet of things (IoT),[295] to name but a very few. The difference that layer-2 makes is that, should a dispute arise, authenticated claims can be submitted to the parent chain to decide the outcome. This makes the solution independent without isolating it from the bigger ecosystem of trust. Similarly, the interoperability-oriented blockchain solutions applied in 'non-crypto' applications offer much more freedom to developers while guaranteeing compatibility between different chains.

Finally, third-generation projects devoted to digital identity and on-chain data management offer additional functionalities for new kinds of projects that were unavailable in the early blockchain systems, such as the possibility of storing essential data right on the chain and allowing them to replicate across the entire network.

While it is hard to predict the future of such a volatile domain of technology, there is also no doubt that the innovative solutions reducing the risk of quantum computers will bring yet another wave of solutions that will only strengthen the position of blockchain technology in the modern digital world.

Conclusions

Five years have passed since we started on our journey to see if and how blockchain technology is being and could be used along the scientific research workflow. We met a lot of blockchain enthusiasts from around the world along the way and learned a great deal from them about the pros and cons of its implementation in science and technology. What we ultimately learned from our interviews is that adoption of the technology is growing globally in general and is accelerating in the life and health sciences.[135] We found that all parts of the scientific research cycle can benefit from the use of distributed ledger technology, and we expect new developments and use cases to continue to emerge. In fact, a report from the Davos 2023 World Economic Forum states that "blockchain technology offers more promises than problems and that as a technology it will continue to grow exponentially, and its use cases expand. The real-world applications of blockchain, many already in use by organizations focused on international development, offer greater utility and cost savings".[42] It should be noted that several nations have now established "Blockchain National Roadmaps," among them the United Kingdom,[296] Australia[297] and Germany[292] (the first nation to do so). More recently (June 2023) Canadian lawmakers recommended that "the Government of Canada, in consultation with the provinces and stakeholders, should establish a national blockchain strategy" to provide a clear policy direction and regulatory approach for blockchain enterprises.[298]

While our focus was blockchain technology usage in science, our journey exposed us to its usage across many industries – finance, law, environment, global trade and commerce, insurance, real estate, media and entertainment, supply chain management, etc. A recent report indicates that most of the top one hundred global companies are adopting the technology to meet their unique needs. These needs rarely involve the use of cryptocurrencies[299] and it is critically important to make the distinction between blockchain technology and cryptocurrency. As reiterated throughout this paper, blockchain is the underlying engine that supports cryptocurrencies. More significantly, it is an engine that can support a diverse array of other, nonfinancial use cases. A recent report indicates that even Amazon, Microsoft, and Google are actively supporting blockchain development and offering services that allow organizations to save money and gain greater efficiencies.[300] The report provides an example of how a blockchain-based solution reduces the letter-of-credit processing time from a few days to a few hours. "The shared, decentralized ledger allows parties to access the documents and make updates in real time, eliminating the need for emailing, faxing, and mailing processes that characterize traditional procedures".[300]

As we look back on when we started our journey, it is obvious that time has not stood still and blockchain technology has evolved considerably. For example, since the launch of Ethereum 2.0[301] on December 1, 2020, a series of planned upgrades have been implemented to mitigate, if not eliminate, the technology's early weaknesses. And, as noted in Section "The Present and Future of Blockchain Technology: Technical Capabilities and

Challenges" of this paper, we are now dealing with the third generation of the technology and experts are well on their way to resolving the issues of scalability, data privacy, data management as well as the interoperability of diverse blockchains in a fourth generation of the technology. We stated on the first page of this white paper that it was ultimately the seamless interoperability of the diverse communication networks that had emerged as a result of ARPANET which gave birth to version one of the internet. It was social media that took the static Web 1.0 to the dynamic Web 2.0, but it will be blockchain technology which will be at the core of taking the internet to the next level – Web 3.0.[302]

While the scope of blockchain technology's impact is difficult to predict since it is still in the early stages of broad adoption, we believe that its future looks bright. Indeed, since we started writing this review, a fundamentally new "way" to do science has blossomed that has blockchain technology at its heart: decentralized science (DeSci). DeSci aims to create a more equitable, efficient, and innovative scientific research ecosystem by leveraging blockchain technology and decentralized networks to create a more open, incentivized, and community-driven scientific research ecosystem.[303] There is not space in this paper to go into any more detail on DeSci, but it is an exciting development in the broader scientific arena and a great example of an emerging blockchain use-case; we urge readers to watch out for it. From a chemical science perspective, it was selected as one of the Top 10 Emerging Technologies in Chemistry in 2021 by IUPAC as noted in the Executive Summary, and a recent report from the European Chemical Industry Council entitled, "Artificial Intelligence and Blockchain: Insights and Actions for the Chemical Industry",[304] boldly states that blockchain technology holds the potential for disruption across the chemical enterprise (refer to that report to learn more about how they see that potential applications in the chemical sciences). The authors of this paper strongly believe that the same can be said for many diverse enterprises.

Four take-home points on blockchain technology

Finally, we would like to give you four take-home points on the key aspects of blockchain technology to remember, separate from how that technology can be applied to the scientific workflow:

- Blockchain is *not* cryptocurrency. Do not let cryptocurrency scandals deter you from learning more about the technology.
- Blockchain is a potential disruptor for all industries, especially where third party intermediaries are involved. Everyone should take this technology seriously and potentially consider using it to their advantage. But…
- Blockchain is *not* a solution in search of a problem; while worth exploring, implementation is not for everyone or for every business challenge. Do your homework first!
- Blockchain has been built on prior technologies, many of which are still essential. It is important to know what has gone before and to continue to build upon the strongest technologies.

Below are also two highly relevant quotes whose individual messages need to be carefully balanced within the context of this paper. These are:

"We are stuck with technology when what we really want is just stuff that works".[305]

And

"We tend to *overestimate* the effect of a technology in the short run and *underestimate* the effect in the long run".[306]

Given the summary above, a word of advice to the reader – do not underestimate the potential of blockchain technology in the long run. Since this technology was selected as one of IUPAC's Top 10 Emerging Technologies in Chemistry in 2021, we hope to continue to monitor blockchain's adoption in chemistry and the emergence of new uses cases and update this white paper in the not-too-distant future. And if, in the meantime you want to learn more about the technology at a more formal level, we refer you to a list of "The Best Universities for Blockchain and Cryptography in the World" that was updated by EduRank in February 2024[307] and a list of reading material in Appendix B Please, do not hesitate to reach out to us with questions, to discuss your own blockchain experience, or to provide input as to what you would like to learn more about this technology. We very much look forward to hearing from you, and our contact information is below.

Acknowledgements: The authors give sincere thanks to the following individuals who gave of their time, met with us, and provided invaluable information without which this paper could not have been written: Dr. Sönke Bartling, Alexander von Humboldt Institute for Internet and Society, Berlin, Germany; Dr. John Domingue, Professor at and Director of the Knowledge Media Institute, Open University, UK; James Lawton, at the time of the interview, Max Planck Digital Library; Dr. Sean Manion, Chief Science Officer, Equideum Health and Editor for Frontiers in Blockchain; Dr. Steve McCloskey, Founder and CEO, Nanome, Inc.; Dr. Naseem Naqvi, President of the British Blockchain Association and Editor-in-Chief of the *Journal of the British Blockchain Association*; Dr. Richard Norman, at the time of the interview, Consultant Project Manager, Pistoia Alliance; Susan Ramonat, at the time of the interview, CEO and Co-Founder, Spiritus Partners; James R. Sacra, at the time of the interview, Vice President of Technology, Nursing, and Healthcare Education, Elsevier; Dr. Joris van Rossum, Director, Research Integrity, International Association of Scientific, Technical and Medical Publishers (STM); Dr. Sandra Vengadasalam, Max Planck Digital Library.
Research ethics: Not applicable.
Informed consent: Not applicable.
Author contributions: All authors have accepted responsibility for the entire content of this manuscript and approved its submission.
Use of Large Language Models, AI and Machine Learning Tools: None declared.
Conflict of interest: The authors state no conflict of interest.
Research funding: None declared.
Data availability: Not applicable.

Appendix A

KnowLedger: trust and the Digital Research Notebook

Stuart Chalk, Professor of Chemistry and Biochemistry, University of North Florida, USA.

The hardbound laboratory notebook has been the bedrock of scientific research. Scientists are taught to create the record of research by writing planned experiments, recording data, processing and evaluating results, and detailing conclusions. In academia, many faculty members require students to use carbon copy notebooks to provide backup of data. In industry, managers sign-off on the work each day and store the notebooks in fire-proof safes as they are the intellectual property (IP) of a company and the definitive evidence for regulatory compliance.

In today's digital scientific enterprise this seems so – arcane. However, while the medium needs changing, the underlying concept – that of creating the definitive record of scientific work – remains the same. In fact, in the digital age it needs to be taken further, as there is a myriad of ways in which data can be manipulated (either deliberate or accidental) and the threat of being scoped (or digitally robbed) is far greater than in previous generations. Consequently, we must approach a new level of trust in the process and in the data that we generate – whether they be positive or negative results.

One of blockchain technology's most touted attributes is that it can create an immutable record, thereby enabling trust. Integrating blockchain into the collection of research data has the potential to revolutionize scientific research and enable scientists to share data more freely as they can definitively prove the development of IP-worthy results. In 2021 the National Institute of Standards and Technology (NIST) funded a research project for the development of a prototype Digital Research Notebook (DRN) system called KnowLedger. The concept is to build a system where research data is captured semantically immediately at birth and stored on a blockchain, incrementally as knowledge is added.

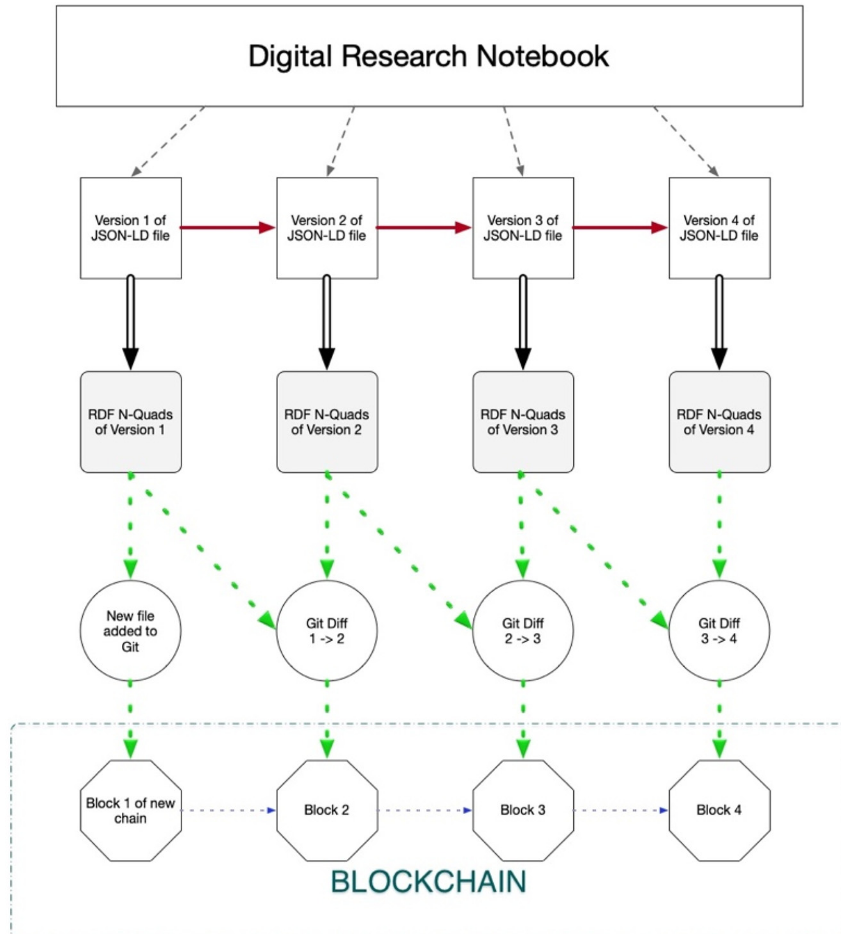

Fig. 6: A blockchain based knowledge evolution system. Legend: ◻ JSON-LD data file, ▢ Text file containing semantic "quads" RDF triples + graph name, ◯ Git 'diff' versioning file (text), ⬡ BlockChain block with added 'Git' file data.

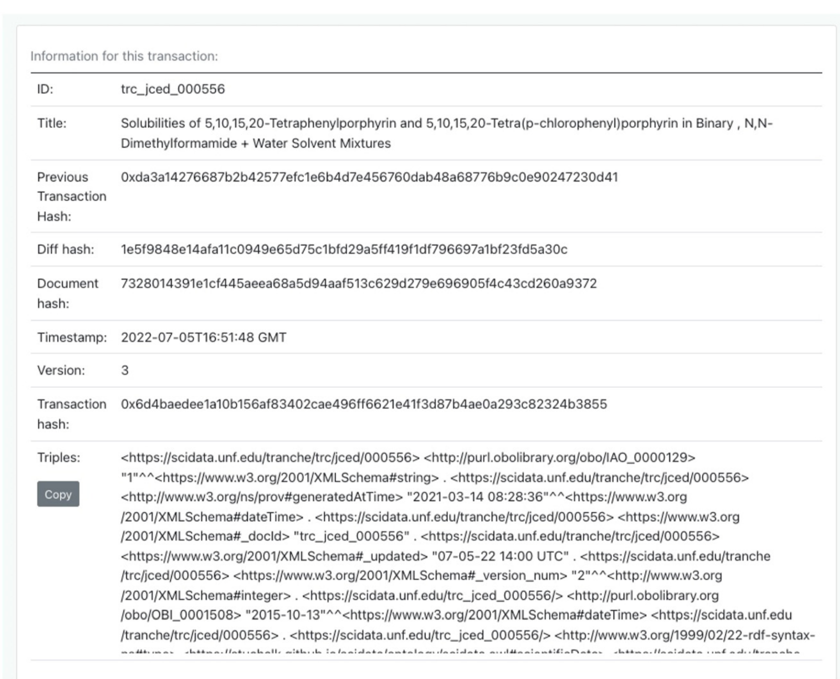

Fig. 7: A blockchain transaction in the knowledge evolution system.

This approach is accomplished by storage of research data entered into the system as JavaScript for Linked Data (JSON-LD) files. JSON-LD is an encoding of the Resource Description Framework (RDF), the format for encoding information as semantic triples, statements of knowledge represented in the Subject-Predicate-Object (SPO) pattern. As data is added, the JSON-LD file stores more knowledge (securely in the browser), is intermittently saved in MongoDB database (JSON-based), and finally converted into the equivalent RDF triples it contains. As each new version is stored in MongoDB it is converted to RDF as a text file that is monitored in real time by the version control software Git. This allows the added knowledge to be generated as a Git "diff" file which contains only those lines (triples) that have been added and deleted. Subsequently, these diff files are used as a "data packet" for a new transaction (one or more blocks) on the Bloxberg Blockchain.[45] The transaction additionally stores the ID of the original JSON-LD file, the ID of the difference file and the hash of the previous transaction (if it is not the first transaction from a file). As a result, a single JSON-LD file is stored as a sequence of blocks on a blockchain and can be regenerated by sequential re-integration of the RDF from a set of file blocks and conversion back to JSON-LD using framing. The evolution of the file could also be displayed as a video allowing other researchers to see how the data was created. This overall process is shown in Fig. 6 and an example block with data is shown in Fig. 7.

Such a knowledge evolution system (KES) would be an important advancement allowing scientists to document their work without concerns of losing data or being scooped. This is achieved by encrypted storage of the JSON-LD file in the browser which is updated as the user performs actions in the interface and intermittent storage of the JSON-LD file in the system with a confirmation of the successful update transaction on a blockchain.

Appendix B

Selected readings/resources

All the material referenced throughout this white paper is worth reading in detail on the topics in which you are interested. This section provides supplemental reading material that provides additional insights.

Blockchain for Dummies, Manav Gupta, 2019, third IBM Limited Edition, John Wiley & Sons, Inc., ISBN: 978-1-119-62196-6 (paperback); ISBM: 978-1-119-62197-3 (e-edition); for the downloadable pdf go to https://www.scribd.com/document/554784492/Blockchain-for-Dummies-3rd-Edition-2019, accessed February 13, 2025.

Blockchain, edited by Sandra Hirsh and Susan Alman, 2020, American Library Association, ISBN: 978-0-8389-1743-5 (paperback), a book in the Library Futures series.

The Business Blockchain: Promise, Practice, and Application of the Next Internet Technology, William Mougayar, Wiley & Sons, 2016, ISBN 978-1-119-30031-1.

Blockchain Revolution, Don Tapscott & Alex Tapscott, Penguin Group (USA) Inc., 2016, ISBN 978-0-241-23785-4.

The Blockchain and the New Architecture of Trust, Kevin Werbach, Massachusetts Institute of Technology, 22018, ISBN 9780262038935.

The Truth Machine: The Blockchain and the Future of Everything, Michael J. Casey and Paul Vigna, St. Martin's Press, 2018, ISBN 978-1-250-11457-0 (hardcover), 978-1-250-11460-0 (e-book).

The Real Business of Blockchain: How Leaders can Create Value in a New Digital Age, David Furlonger and Christophe Uzureau, Harvard Business Review Press, copyright Gartner, Inc., 2019, ISBN: 978-1-63369-804-8.

Blockchain: Blueprint for a New Economy, Melanie Swan, O'Reilly Media Inc., 2015. ISBN: 978-1-491-92049-7.

Mastering Bitcoin: Unlocking Digital Cryptocurrencies, Andreas M. Antonopoulos. Originally published by O'Reilly Media Inc., 2014. ISBN 978-1-449-37404-4. Available as pdf online: https://pdfstop.com/mastering-bitcoin-epub/, accessed August 6, 2023.

References

1. Fankenfield, J. Distributed Ledger Technology (DLT): Definition and How it Works (Investopedia). https://www.investopedia.com/terms/d/distributed-ledger-technology-dlt.asp (Accessed 2024-07-27).
2. Harris, M. How Blockchain is Transforming Grants Management. https://governmentciomedia.com/how-blockchain-transforming-federal-grants-management (Accessed 2024-07-27).
3. Malone, K. Blockchain Saving HHS $30M on First Accelerate Contract. https://www.meritalk.com/articles/blockchain-saving-hhs-30m-on-first-accelerate-contract (Accessed 2024-07-27).
4. Leiner, B. M.; Cerf, V. G.; Clark, D. D.; Kahn, R. E.; Kleinrock, L.; Lynch, D. C.; Postelo, J.; Roberts, L. G.; Wolff, S. Brief History of the Internet, Internet Society. https://www.internetsociety.org/resources/doc/2017/brief-history-internet/ (Accessed 2024-07-27).
5. BitCoin. What is BitCoin? https://www.bitcoin.com/get-started/what-is-bitcoin/ (Accessed 2024-07-27).
6. Davies, S. How Bitcoin and its Blockchain Works. https://www.ft.com/video/2be94381-66dc-3320-a292-6a1cde0a3d5f (Accessed 2024-07-27).
7. Wikipedia. Bankruptcy of FTX. https://en.wikipedia.org/wiki/Bankruptcyof_FTX (Accessed 2024-07-27).
8. Casey, N. J.; Vigna, P. *MIT Technol. Rev.* **2018**, *121*, 10–16. https://www.technologyreview.com/2018/04/09/3066/in-blockchain-we-trust/ (Accessed 2024-07-27).
9. Wikipedia. Double Entry Bookkeeping. https://en.wikipedia.org/wiki/double_entry_bookkeeping (Accessed 2024-07-27).
10. Rega, F. G. From Double-Entry Bookkeeping to the Blockchain: The New Financial Infrastructure. https://www.fintastico.com/blog/double-entry-bookkeeping-blockchain-new-financial-infrastructure/ (Accessed 2024-07-27).
11. Yaga, D.; Mell, P.; Roby, N.; Scarfone, K. NISTIR 8202 Blockchain Technology Overview. https://doi.org/10.6028/NIST.IR.8202 (Accessed 2024-07-27).
12. AJustice. Blockchain 101 Beginners Guide to Understanding the Technology. https://medium.com/coinmonks/blockchain-101-beginners-guide-to-understanding-the-technology-75a75f863ec2 (Accessed 2024-07-27).
13. Gupta, M. *Blockchain for Dummies* 2020, 7. https://aldovidales.com/wp-content/uploads/2021/12/Blockchain-for-Dummies-3rd-Edition-2019-1.pdf (Accessed 2024-07-27).
14. Wikipedia. Proof of Work. https://en.wikipedia.org/wiki/proof_of_work (Accessed 2024-07-27).
15. Wikipedia. Proof of Stake. https://en.wikipedia.org/wiki/proof_of_stake (Accessed 2024-07-27).
16. Ethereum. Proof of Stake (PoS). https://ethereum.org/en/developers/docs/consensus-mechanisms/pos/ (Accessed 2024-07-27).
17. Aman, J. A. S., Proof of Work vs Proof of State: Which one is Better? https://www.bitdegree.org/crypto/tutorials/proof-of-work-vs-proof-of-stake (Accessed 2024-07-27).
18. Britannica. Trust. https://www.britannica.com/dictionary/trust (Accessed 2024-07-27).
19. Furlonger, D.; Uzureau, C. *The Real Business of Blockchain: How Leaders can Create Value in a New Digital Age*; Harvard Business Review Press: Boston, Massachusetts, USA, 2019. https://www.gartner.com/en/publications/the-real-business-of-blockchain (Accessed 2024-07-27).
20. Smith, H. Blockchain as a Platform for Data Governance 2.0 (The Data School). https://www.dataschool.com/data-conversations/blockchain-as-a-platform-for-data-governance-2-0/ (Accessed 2024-07-27).
21. Ledger.com. What are Public Keys vs Private Keys? https://www.ledger.com/academy/blockchain/what-are-public-keys-and-private-keys/ (Accessed 2024-07-27).
22. Werbach, K. *The Blockchain and the New Architecture of Trust*; MIT Press, 2018. https://mitpress.mit.edu/9780262547161/the-blockchain-and-the-new-architecture-of-trust/ (Accessed 2024-07-27).
23. Wikipedia. Merkle Tree. https://en.wikipedia.org/wiki/merkle_tree (Accessed 2024-07-27).
24. Iredale, G. History of Blockchain Technology: A Detailed Guide. https://101blockchains.com/history-of-blockchain-timeline/ (Accessed 2024-07-27).
25. Lytovchenko, A. The History of Blockchain: From Establishment to Broad Adoption. https://eleks.com/blog/the-history-of-blockchain/ (Accessed 2024-07-27).
26. Surety Blockchain. Surety: The Power of Proof. https://suretyblockchain.com/ (Accessed 2024-07-27).
27. Nakamoto, S. Bitcoin: A Peer-to-Peer Electronic Cash System. https://www.bitcoin.com/bitcoin.pdf (Accessed 2024-07-27).
28. Haber, S.; Stornetta, W. S. How to Time-Stamp a Digital Document. *J. Cryptol.* **1991**, *3*, 99–111. https://doi.org/10.1007/BF00196791 (Accessed 2024-07-27).
29. Wikipedia. Ralph Merkle. https://en.wikipedia.org/wiki/ralph_merkle (Accessed 2024-07-27).
30. Redman, J. Bitcoin's Creator Satoshi Nakamoto is Now a Member of the Top 20 World's Richest People. https://news.bitcoin.com/bitcoins-creator-satoshi-nakamoto-now-a-member-top-20-worlds-richest-people/ (Accessed 2024-07-27).
31. Browne, R. Ethereum: What is it and how is it Different from Bitcoin. https://www.cnbc.com/2021/05/10/ethereum-what-is-it-and-how-is-it-different-to-bitcoin.html (Accessed 2024-07-27).
32. Frank, J.; Silverstein, S. Etherium: How was it Created and Why? https://insider.com/vitalik-buterin-created-ethereum-one-of-the-worlds-three-largest-cryptocurrencies-2019-1?r=US&IR=T (Accessed 2024-07-27).
33. IBM. What are Smart Contracts on a Blockchain? https://www.ibm.com/topics/smart-contracts (Accessed 2024-07-27).

34. Millman, R. What is Ethereum 2.0? Ethereum's Consensus Layer and Merge Explained. https://decrypt.co/resources/what-is-ethereum-2-0 (Accessed 2024-07-27).
35. Nambiampurath, R. What is Ethereum 2.0? https://www.investopedia.com/ethereum-2-0-6455959 (Accessed 2024-07-27).
36. Hyperledger Foundation. Building Better Together. https://www.hyperledger.org (Accessed 2024-07-27).
37. Tse, S. Blockchain Interoperability: Why it Matters and How to Make it Happen. https://readwrite.com/blockchain-interoperability-why-it-matters-and-how-to-make-it-happen/ (Accessed 2024-07-27).
38. Gent, E. How Can We Get Blockchains to Talk to Each Other? https://spectrum.ieee.org/blockchain-interoperability (Accessed 2024-07-27).
39. Polkadot, Polkadot Decentralized Blockchain. https://polkadot.network (Accessed 2024-07-27).
40. Cosmos, Cosmos Build on the Interchain. https://cosmos.network (Accessed 2024-07-27).
41. Harmony ONE, https://harmony.one (Accessed 2024-07-27).
42. Nath, A. In Davos, Blockchain Yields More Promises Than Problems. https://www.coindesk.com/opinion/2023/01/18/in-davos-blockchain-yields-more-promises-than-problems/ (Accessed 2024-07-27).
43. Craiyon LLC. Craiyon: AI Image Generator Tool. https://www.craiyon.com (Accessed 2024-07-27).
44. Artifacts. ARTiFACTS: Validating Evidence for Science and Commerce. https://artifacts.ai (Accessed 2024-07-27).
45. Max Planck Society. First International Blockchain for Science: Bloxberg. https://www.mpg.de/13417668/first-international-blockchain-for-science-bloxberg (Accessed 2024-07-27).
46. Artifacts. ARTiFACTS: Verify: Drug quality Monitoring Across the Pharmaceutical Supply. https://artifacts.ai/verify/ (Accessed 2024-07-27).
47. IP LEVERAGED SAS. Bernstein: Blockchain for Intellectual Property. https://www.bernstein.io (Accessed 2024-07-27).
48. MPS. A portrait of the Max Planck Society. https://www.mpg.de/short-portrait (Accessed 2024-07-27).
49. Hodl, J. What is The Blockchain? https://www.whatisbitcoin.com/blockchain (Accessed 2024-07-27).
50. MPDL. First International Blockchain for Science: Bloxberg. https://www.mpg.de/13417668/first-international-blockchain-for-science-bloxberg (Accessed 2024-07-27).
51. MPDL. Bloxberg: The Blockchain for Science – Whitepaper 2.0, 2022. https://bloxberg.org/wp-content/uploads/2022/07/bloxberg_whitepaper_2.0.pdf (Accessed 2024-07-27).
52. MPDL. Fourth Bloxberg Summit. https://www.mpdl.mpg.de/ueber/presse/812-fourth-bloxberg-summit-2022.html (Accessed 2024-07-27).
53. Proof of Existence. Written Forever. https://proofofexistence.com (Accessed 2024-07-27).
54. Stampery. Blockchain-Based Data Certification. https://www.stampery.com (Accessed 2024-07-27).
55. Stampery. Stampery Blockchain Timestamping Architecture (BTA). https://s3.amazonaws.com/stampery-cdn/docs/Stampery-BTA-v6-whitepaper.pdf (Accessed 2024-07-27).
56. LinkedIn. Scienceroot: The Future of Science is Here. https://www.linkedin.com/company/scienceroot/ (Accessed 2024-07-27).
57. DEIP. Creator Economy. https://deip.world/creator-economy/ (Accessed 2024-07-27).
58. MEXC MEXC AMA DEIP Protocol. https://blog.mexc.com/mexc-ama-deip-protocol-session-with-alex-shkor/ (Accessed 2024-07-27).
59. Coinbase. What is a Non-Fungible Token (NFT)? https://www.coinbase.com/learn/crypto-basics/what-are-nfts (Accessed 2024-07-27).
60. DEIP. The Story so Far. https://deip.world (Accessed 2024-07-27).
61. DEIP. What Can You Build on DEIP? Six Projects Being Built Now. https://web.archive.org/web/20230203074917/https://learn.deip.world/what-can-you-build-on-deip-six-projects-being-built-now (Accessed 2024-07-27).
62. Nanome. The Future of Moelcular Design. https://nanome.ai (Accessed 2024-07-27).
63. Company, M. What is Tokenization? https://www.mckinsey.com/featured-insights/mckinsey-explainers/what-is-tokenization (Accessed 2024-11-01).
64. McCloskey, S.; Funakawa, K.; Brumet, V.; Morgan, S.; Leija, E.; Simon, A.; Lee, K.; Howard, M. MATRYX – Innovation Ecosystem Built on the Blockchain, 2019. https://nanome.ai/downloads/matryx-whitepaper.pdf (Accessed 2024-07-27).
65. Molecule. The Future of Medicine Belongs to Everyone. https://www.molecule.xyz (Accessed 2024-07-27).
66. Investopedia. Non-Fungible Token (NFT): What it Means and How it Works. https://www.investopedia.com/non-fungible-tokens-nft-5115211 (Accessed 2024-07-27).
67. Golato, T. IP-NFTs for Researchers: A New Biomedical Funding Paradigm. https://medium.com/molecule-blog/ip-NFTs-for-research-a-new-biomedical-finding-paradigm-91312d8d92e6 (Accessed 2024-07-27).
68. Molecule. Molecule's First IP-NFT for Drug Discovery R&D in the United States. https://www.molecule.xyz/blog/molecules-first-ip-nft-in-the-united-states (Accessed 2024-07-27).
69. Ryan, F. How HHS is Transforming Grants Management. https://governmentciomedia.com/how-hhs-transforming-grants-management (Accessed 2024-07-27).
70. US Treasury. Transformation Stories: Blockchain and the (Possible) Future of Federal Grant Management. https://fmvision.fiscal.treasury.gov/blockchain-and-the-possible-future-of-federal-grant-management.html (Accessed 2024-07-27).
71. Kishore, S.; Chan, J.; Muthupoltotage, U. P.; Young, N.; Sundaram, D. Blockchain-Based Micro-credentials: Design, Implementation, Evaluation, and Adoption. In *54th Hawaii International Conference on System Sciences*; Hawaii, US, 2021; p. 6846. http://hdl.handle.net/10125/71442 (Accessed 2024-07-27).
72. Hashed Health. A Venture Studio Driving Innovation and Collaboration in Healthcare. https://hashedhealth.com (Accessed 2024-07-27).

73. Gaynor, M.; Tuttle-Newhall, J.; Parker, J.; Patel, A.; Tang, C. Adoption of Blockchain in Health Care. *J. Med. Internet Res.* **2020**, *22*, e17423; https://doi.org/10.2196/17423.
74. Sivagnanam, S.; Nandigam, V. CICI: RDP: Open Science Chain (OSC) – A Novel Distributed Ledger-Based Framework for Protecting Integrity and Provenance of Research Data, 2018. https://www.nsf.gov/awardsearch/showAward?AWD_ID=1840218 (Accessed 2024-07-27).
75. USCD. Protecting Integrity and Provenance of Research Data. https://opensciencechain.org (Accessed 2024-07-27).
76. Microsoft. GitHub: Let's Build from Here. https://github.com (Accessed 2024-07-27).
77. Bruch, K. M. SDSC's Open Science Chain Awarded $500,000 NSF Grant. https://www.sdsc.edu/News%20Items/PR20210803_opensciencechain.html (Accessed 2024-07-27).
78. Sivagnanam, S.; Nandigam, V.; Lin, K. Introducing the Open Science Chain. In *Proceedings of the Practice and Experience in Advanced Research Computing on Rise of the Machines (learning)*, 2019; pp. 1–5.
79. Project Jupyter. Free Software, Open Standards, and Web Services for Interactive Computing Across All Programming Languages. https://jupyter.org (Accessed 2024-07-27).
80. Driscoll, M. Jupyter Notebook: An Introduction. https://realpython.com/jupyter-notebook-introduction (Accessed 2024-07-27).
81. Deepyr Tech. Interacting With Ethereum Using web3.py and Jupyter Notebooks. https://medium.com/deepyr/interacting-with-ethereum-using-web3-py-and-jupyter-notebooks-e4207afa0085 (Accessed 2024-07-27).
82. Labii. An All-in-One Platform for all Your Research Data. https://www.labii.com (Accessed 2024-07-27).
83. Allen, M. D. Family Tree of Data – Provenance and Neo4J. https://www.slideshare.net/MDavidAllen1/family-tree-of-data-provenance-and-neo4j-46405323 (Accessed 2024-07-27).
84. Chowdhury, M. Why is Blockchain the Next Big Thing for Data Science? https://www.analyticsinsight.net/why-is-blockchain-the-next-big-thing-for-data-science (Accessed 2024-07-27).
85. Pansare, A. What Makes Blockchain and Data Science a Perfect Combination. https://www.linkedin.com/pulse/what-makes-blockchain-data-science-perfect-anand-pansare/ (Accessed 2024-07-27).
86. Mastitsky, S. Data Science for Blockchain: Understanding the Current Landscape. https://towardsdatascience.com/data-science-for-blockchain-understanding-the-current-landscape-c136154c367e (Accessed 2024-07-27).
87. Voshmgir, S. Blockchain Solutions for Scientific Publishing. https://medium.com/crypto3conomics/blockchain-solutions-for-scientific-publishing-ef4b4e79ae2 (Accessed 2024-07-27).
88. van Rossum, J.; Lawlor, B. *Information Services & Use*, Vol. 38, 2018; pp. 95–98; https://doi.org/10.3233/isu-180003.
89. Enago Academy. The Importance of Scientific Transparency and Reproducibility. https://www.enago.com/academy/the-importance-of-scientific-transparency-and-reproducibility (Accessed 2024-07-27).
90. Baker, M. 1,500 Scientists Lift the Lid on Reproducibility. *Nature* **2016**, *533*, 452–454; https://doi.org/10.1038/533452a.
91. Ioannidis, J. P. A. Why Most Published Research Findings Are False. *PLoS Med.* **2005**, *2*, e124; https://doi.org/10.1371/journal.pmed.0020124.
92. BBA. JBBA Launches Blockchain Based Ledger of Record for Research in Collaboration with ARTiFACTS. https://britishblockchainassociation.org/jbba-launches-blockchain-based-ledger-of-record-for-research-in-collaboration-with-artifacts (Accessed 2024-07-27).
93. JBBA. ARTiFACTS Blockchain Portal. https://jbba.scholasticahq.com/pages/96-blockchain-metadata (Accessed 2024-07-27).
94. BBA. The British Blockchain Association. https://britishblockchainassociation.org (Accessed 2024-07-27).
95. BBA. The Journal of The British Blockchain Association. https://jbba.scholasticahq.com (Accessed 2024-07-27).
96. WebWire. Partners in Digital Health Launches Blockchain Based Ledger of Record for Research in Collaboration with ARTiFACTS. https://www.webwire.com/ViewPressRel.asp?aId=259283 (Accessed 2024-07-27).
97. Bloxberg. Bloxberg Peer Review. https://github.com/bloxberg-org/peer-review-app (Accessed 2024-07-27).
98. POLP. Ledger. https://ledgerjournal.org/ojs/ledger (Accessed 2024-07-27).
99. Lawlor, B. An Overview of the NFAIS 2017 Annual Conference: The Big Pivot: Re-Engineering Scholarly Communication. *Inf. Serv. Use* **2017**, *37*, 283–306; https://doi.org/10.3233/isu-170854.
100. Orvium. Streamline Your Scientific Publishing Process. https://orvium.io (Accessed 2024-07-27).
101. Orvium. Orvium Becomes CERN's Spinoff. https://blog.orvium.io/orvium-becomes-cerns-spin-off (Accessed 2024-07-27).
102. Zenodo. About Zenodo. https://about.zenodo.org (Accessed 2024-07-27).
103. CERN. Invenio. https://kt.cern/technologies/invenio (Accessed 2024-07-27).
104. CERN. Orvium. https://kt.cern/startups/orvium (Accessed 2024-07-27).
105. Orvium. The Evolving Scholar First Orvium Community for Open Science. https://blog.orvium.io/the-evolving-scholar (Accessed 2024-07-27).
106. Orvium. 7 Benefits of Blockchain in Publishing Platforms. https://blog.orvium.io/benefits-of-blockchain (Accessed 2024-07-27).
107. Pluto. Innovate Innovations. https://pluto.im (Accessed 2024-07-27).
108. Katalysis, https://medium.com/katalysis-io (Accessed 2024-07-27).
109. Principia. Decentralize Peer Review. https://web.archive.org/web/20220409144322/http://principia.network/ (Accessed 2024-07-27).
110. Frankl. *Open Science on the Blockchain*. https://frankl.io (Accessed 2024-07-27).
111. BPPP. Towards a Fairer and More Transparent Peer Review Ecosystem. https://web.archive.org/web/20220302155958/https://www.blockchainpeerreview.org/ (Accessed 2024-07-27).

112. Ilovephd. Learn to Publish in This New Decentralized Publication. https://www.ilovephd.com/what-is-pluto-research-network-learn-to-publish-in-blockchain-technology-based-decentralized-publication/ (Accessed 2024-07-27).
113. Scisets, Transparent, Trustworthy, Decentralized and Collaborative for Science and Research. https://docs.scisets.com/overview/what-is-scisets-ra (Accessed 2024-07-27).
114. Gunter, D. *Transforming Scholarly Publishing With Blockchain Technologies and AI*; IGI Global: Hershey, PA, 2021.
115. Freedman, L. P.; Cockburn, I. M.; Simcoe, T. S. The Economics of Reproducibility in Preclinical Research. *PLOS Biol.* **2015**, *13*, e1002165; https://doi.org/10.1371/journal.pbio.1002165.
116. Drolet, B. C.; Lorenzi, N. M. Translational Research: Understanding the Continuum from Bench to Bedside. *Transl. Res.* **2011**, *157*, 1–5; https://doi.org/10.1016/j.trsl.2010.10.002.
117. Manion, S. Enhancing Federal Research: Traumatic Brain Injury & Blockchain Technology – Part 1.5, The Why. https://www.linkedin.com/pulse/enhancing-federal-research-traumatic-brain-injury-part-sean-manion-1/ (Accessed 2024-07-27).
118. Ramnani, M. Walmart-MediLedger Partnership: Leveraging Blockchain for Pharmaceutical Tracking. https://www.mediledger.com (Accessed 2024-07-27).
119. Mulcahy, N. Cancer Drug Recyclers Chosen for FDA Pilot. https://www.medscape.com/viewarticle/912383 (Accessed 2024-07-27).
120. UND. Lieberman Lab Partners with Blockchain-Based Platform to Track Real-Time Chain-of-custody Throughout Pharmaceutical Supply Chain. https://science.nd.edu/news-and-media/news/lieberman-lab-partners-with-blockchain-based-platform-to-track-real-time-chain-of-custody-throughout-pharmaceutical-supply-chain/ (Accessed 2024-07-27).
121. PLA. The PharmaLedger Association: Building a Digital Trust Ecosystem for Healthcare. https://pharmaledger.org/ (Accessed 2024-07-27).
122. EU. Horizon 2020/Europe. https://research-and-innovation.ec.europa.eu/funding/funding-opportunities/funding-programmes-and-open-calls/horizon-europe_en (Accessed 2024-07-27).
123. PLA. PharmaLedger Association Announces First Product and Members. https://pharmaledger.org/pharmaledger-press-release (Accessed 2024-07-27).
124. Pistoia Alliance. Informed Consent Blockchain. https://www.pistoiaalliance.org/projects/current-projects/informed-consent-blockchain/ (Accessed 2024-07-27).
125. Pistoia Alliance. The Pistoia Alliance Calls on Life Science and Healthcare Ecosystems to Restructure Around Patient Centricity. https://pistoiaalliance.org/news/driving-patient-centricity-in-rd-2022 (Accessed 2024-07-27).
126. R. Norman, Personal Communication (**2022**)
127. Drug Discovery World. Decentralised Identities: Blockchain Based Informed Consent'. https://www.ddw-online.com/decentralised-identities-blockchain-based-informed-consent-2-28520-202402 (Accessed 2024-11-01).
128. Hang, L.; Chen, C.; Zhang, L.; Yang, J. Blockchain for Applications of Clinical Trials: Taxonomy, Challenges, and Future Directions. *IET Commun.* **2022**, *16*, 2371–2393; https://doi.org/10.1049/cmu2.12488.
129. Henderson, C. Napier University to Demonstrate Assurance Layer for Medical Devices. https://www.digit.fyi/napier-university-health-tech (Accessed 2024-07-27).
130. Carfax. CARFAX Vehicle History Reports. https://www.carfax.com (Accessed 2024-07-27).
131. Spiritus. Spiritus: Better Together. https://www.spirituspartners.com (Accessed 2024-07-27).
132. Med-Tech. Hospitals Trial Blockchain Tracking of Medical Devices. https://www.med-technews.com/news/hospitals-trial-blockchain-tracking-of-medical-devices (Accessed 2024-07-27).
133. Culinda. Medical Device & IoMT Cyber Security. https://www.culinda.io/iomt-security-assessment (Accessed 2024-07-27).
134. Culinda. Culinda Inc: Safeguarding Health by Securing Devices. https://cybersecurity.cioreview.com/vendor/2019/culinda_inc (Accessed 2024-07-27).
135. Zagadailov, E. Blockchain Applications in Healthcare: A Review of the Health Data Exchange Landscape. https://medium.com/@erin.zagadailov/blockchain-applications-in-healthcare-a-review-of-the-health-data-exchange-landscape-a911f40d42c1 (Accessed 2024-07-27).
136. Blockcerts. About Blockcerts. https://www.blockcerts.org/about.html (Accessed 2024-07-27).
137. Hyland. Hyland Acquires Blockchain-Credentialing Provider Learning Machine. https://www.hyland.com/en/company/newsroom/hyland-acquires-blockchain-credentialing-provider-learning-machine (Accessed 2024-07-27).
138. Cant, J. Malaysian Ministry of Education Fights Fake Degrees With Blockchain Tech. https://cointelegraph.com/news/malaysian-ministry-of-education-fights-fake-degrees-with-blockchain-tec (Accessed 2024-07-27).
139. Wikipedia. Open University. https://en.wikipedia.org/wiki/open_university (Accessed 2024-07-27).
140. Solid. Solid: Your Data, Your Choice. https://solidproject.org (Accessed 2024-07-27).
141. QualiChain. About QualiChain. https://qualichain-project.eu/about (Accessed 2024-07-27).
142. Kokkinakos, P. QualiChain: Decentralised Qualifications' Verification and Management for Learner Empowerment, Education Reengineering and Public Sector Transformation. https://alfresco.epu.ntua.gr/share/s/-eTjAueIQ5-9mH_G2Om0nQ (Accessed 2024-07-27).
143. Domingue, J. What is Blockchain? https://www.open.edu/openlearn/science-maths-technology/computing-ict/what-blockchain (Accessed 2024-07-27).
144. Ivanontech. Blockchain and Digital Identity: What is Digital Identity and Why Do We Need It? https://academy.moralis.io/blog/blockchain-and-digital-identity-what-is-digital-identity-and-why-do-we-need-it (Accessed 2024-07-27).

145. Geroni, D. Self-Sovereign Identity: The Ultimate Beginners Guide!. https://101blockchains.com/self-sovereign-identity (Accessed 2024-07-27).
146. Betz, B. Avast Acquires Self-Sovereign Identity Firm Evernym for Undisclosed Amount. https://www.coindesk.com/business/2021/12/09/avast-acquires-self-sovereign-identity-firm-evernym-for-undisclosed-amount/ (Accessed 2024-07-27).
147. Spherity. Credentialing the World for a New Internet Age with Digital Trust. https://spherity.com (Accessed 2024-07-27).
148. European Commission. Shaping Europe's Digital Future: eIDAS Regulation. https://digital-strategy.ec.europa.eu/en/policies/eidas-regulation (Accessed 2024-11-01).
149. Klumpers, E. Blockchain for Peer Review Architecture (Proof of Concept). https://medium.com/katalysis.io/blockchain-for-peer-review-architecture-proof-of-concept-a60a138a63a7 (Accessed 2024-07-27).
150. Clarivate. Publons (requires login to Web of Science). https://webofscience.help.clarivate.com/Content/publons.html (Accessed 2024-07-27).
151. European Science Foundation. Why Plan S? https://www.coalition-s.org/why-plan-s/ (Accessed 2024-07-27).
152. Ennov. Ennov Acquires MACRO from Elsevier to Reinforce its Leadership Position in the EDC Field. https://en.ennov.com/news/announcement/macro-elsevier-acquisition (Accessed 2024-07-27).
153. Wikipedia. Right to be Forgotten. https://en.wikipedia.org/wiki/right_to_be_forgotten (Accessed 2024-07-27).
154. Intersoft Consulting. General Data Protection Regulation GDPR. https://gdpr-info.eu (Accessed 2024-07-27).
155. BBA. Center for Evidence-Based Blockchain (CEBB). https://britishblockchainassociation.org/cebb/ (Accessed 2024-07-27).
156. Naqvi, N. Evidence-Based Blockchain: Findings from a Global Study of Blockchain Projects and Start-up Companies. *J. British Blockchain Assoc.* **2020**, *3*, 1–13; https://doi.org/10.31585/jbba-3-2-(8)2020.
157. Clarisse. Difference Between Legislation and Regulation. https://www.differencebetween.com/difference-between-legislation-and-regulation (Accessed 2024-07-27).
158. Kereibayev, O. Crypto Regulations in the US – A Complete Guide, 2023. https://sumsub.com/blog/crypto-regulations-in-the-us-a-complete-guide-2023 (Accessed 2024-07-27).
159. Bloomberg Law. Cryptocurrency Laws and Regulations by State. https://pro.bloomberglaw.com/brief/cryptocurrency-laws-and-regulations-by-state (Accessed 2024-07-27).
160. Wikipedia. BitLicense. https://en.wikipedia.org/wiki/BitLicense (Accessed 2024-07-27).
161. Brett, J. Congress Has Now Introduced 32 Crypto And Blockchain Bills. https://www.forbes.com/sites/jasonbrett/2020/04/28/congress-has-introduced-32-crypto-and-blockchain-bills-for-consideration-in-2019-2020 (Accessed 2024-07-27).
162. Nambiampurath, R.; Baird, K. US Congress Introduced 35 Crypto-Related Bills in 2021. https://beincrypto.com/us-congress-35-crypto-related-bills-2021/ (Accessed 2024-07-27).
163. US Congress. H.R. 3543 (117th): Blockchain Technology Coordination Act of 2021, 2021. https://www.govtrack.us/congress/bills/117/hr3543 (Accessed 2024-07-27).
164. US Congress. H.R. 3639 (117th): Blockchain Innovation Act, 2021. https://www.govtrack.us/congress/bills/117/hr3639 (Accessed 2024-07-27).
165. US Congress. S. 1869 (117th): Blockchain Promotion Act of 2021, 2021. https://www.govtrack.us/congress/bills/117/s1869 (Accessed 2024-07-27).
166. US Congress. H.R. 1747: Blockchain Regulatory Certainty Act, 2023. https://www.govtrack.us/congress/bills/118/hr1747 (Accessed 2024-07-27).
167. US Congress. H.R. 1460: Crypto-Asset Environmental Transparency Act of 2023, 2023. https://www.govtrack.us/congress/bills/118/hr1460 (Accessed 2024-07-27).
168. Insider. How the Laws & Regulations Affecting Blockchain Technology and Cryptocurrencies, Like Bitcoin, Can Impact its Adoption. https://www.businessinsider.com/blockchain-cryptocurrency-regulations-us-global?r=US&IR=T (Accessed 2024-07-27).
169. Wikipedia. Mt. Gox. https://en.wikipedia.org/wiki/Mt._Gox (Accessed 2024-07-27).
170. Hertig, A. What Is DeFi? https://www.coindesk.com/what-is-defi (Accessed 2024-07-27).
171. Vermaak, W. MiCA: A Guide to the EU's Proposed Markets in Crypto-Assets Regulation. https://www.sygna.io/blog/what-is-mica-markets-in-crypto-assets-eu-regulation-guide (Accessed 2024-07-27).
172. US SEC. Cryptocurrency/ICOs. https://www.sec.gov/ICO (Accessed 2024-07-27).
173. Coinbase. What is a Stablecoin? https://www.coinbase.com/learn/crypto-basics/what-is-a-stablecoin (Accessed 2024-07-27).
174. Techtelegraph. How the Howey Test Determines if Crypto Assets and NFTs are Securities. https://www.techtelegraph.co.uk/how-the-howey-test-determines-if-crypto-assets-and-nfts-are-securities (Accessed 2024-07-27).
175. Jones, N. How Scientists are Embracing NFTs. *Nature* **2021**, *594*, 481–482; https://doi.org/10.1038/d41586-021-01642-3.
176. BitCoin Wiki. Privacy. https://en.bitcoin.it/wiki/Privacy (Accessed 2024-07-27).
177. Oettler, M. Anonymity vs Pseudonymity. https://blockchain-academy.hs-mittweida.de/courses/blockchain-introduction-technical-beginner-to-intermediate/lessons/lesson-4-privacy-in-blockchain-2/topic/anonymity-vs-pseudonymity (Accessed 2024-07-27).
178. Antonopoulos, A. M. *Mastering Bitcoin*; O'Reilly Media Inc., 2017. https://free.epubebooks.net/ebooks/books/mastering-bitcoin.pdf (Accessed 2024-07-27).
179. Lavrenov, D. A Zero-Knowledge Proof: Improving Privacy on a Blockchain. https://www.altoros.com/blog/zero-knowledge-proof-improving-privacy-for-a-blockchain (Accessed 2024-07-27).
180. BitCoin Wiki. CoinJoin. https://en.bitcoin.it/wiki/CoinJoin (Accessed 2024-07-27).

181. Frankenfield, J. General Data Protection Regulation (GDPR) Definition and Meaning. https://www.investopedia.com/terms/g/general-data-protection-regulation-gdpr.asp (Accessed 2024-07-27).
182. Lewis, N. What Is Metadata? https://www.howtogeek.com/815069/what-is-metadata (Accessed 2024-07-27).
183. EPRS. Blockchain and the General Data Protection Regulation: Can Distributed Ledgers be Squared with European Data Protection law? https://www.europarl.europa.eu/RegData/etudes/STUD/2019/634445/EPRS_STU(2019)634445_EN.pdf (Accessed 2024-07-27).
184. Shute, R. E. Blockchain Technology in Drug Discovery: Use-Cases in R&D. https://www.ddw-online.com/blockchain-technology-in-drug-discovery-use-cases-in-rd-741-201710 (Accessed 2024-07-27).
185. Friedl, S. An Illustrated Guide to Cryptographic Hashes. http://unixwiz.net/techtips/iguide-crypto-hashes.html (Accessed 2024-07-27).
186. QaamGo Media GmbH. Convert Hashes Online. https://hash.online-convert.com (Accessed 2024-07-27).
187. Gürkaynak, G.; Yılmaz, İ.; Yeşilaltay, B.; Bengi, B. Intellectual Property Law and Practice in the Blockchain Realm. *Comput. Law Secur. Rev.* **2018**, *34*, 847–862; https://doi.org/10.1016/j.clsr.2018.05.027.
188. Clark, B.; McKenzie, B. Blockchain and IP Law: A Match Made in Crypto Heaven? https://www.wipo.int/wipo_magazine/en/2018/01/article_0005.html (Accessed 2024-07-27).
189. Rose, A. Blockchain: Transforming the Registration of IP Rights and Strengthening the Protection of Unregistered IP Rights. https://www.wipo.int/wipo_magazine_digital/en/2020/article_0002.html (Accessed 2024-07-27).
190. CBC. Congressional Blockchain Caucus. https://congressionalblockchaincaucus-schweikert.house.gov (Accessed 2024-07-27).
191. BIPC Blog: A Blockchain Innovators Guide to IP Policy. https://digitalchamber.org/a-blockchain-innovators-guide-to-ip-policy (Accessed 2024-07-27).
192. US FDA. What Does FDA do? https://www.fda.gov/about-fda/what-we-do (Accessed 2024-07-27).
193. US FDA. FDA's Technology Modernization Action Plan (TMAP). https://www.fda.gov/media/130883/download (Accessed 2024-07-27).
194. US FDA. FDA Takes New Steps to Adopt More Modern Technologies for Improving the Security of the Drug Supply Chain Through Innovations That Improve Tracking and Tracing of Medicines. https://www.fda.gov/news-events/press-announcements/fda-takes-new-steps-adopt-more-modern-technologies-improving-security-drug-supply-chain-through (Accessed 2024-07-27).
195. IBM. FDA DSCSA Blockchain Interoperability Pilot Project Report. https://www.ibm.com/downloads/cas/9V2LRYG5 (Accessed 2024-07-27).
196. Moosavi, J.; Naeni, L. M.; Fathollahi-Fard, A. M.; Fiore, U. Blockchain in supply chain management: a review, bibliometric, and network analysis.. *Environ. Sci. Pollut. Res.* **2021**, https://doi.org/10.1007/s11356-021-13094-3.
197. IBM. IBM Supply Chain Intelligence Suite: Food Trust. https://www.ibm.com/blockchain/solutions/food-trust (Accessed 2024-07-27).
198. Choudhary, A. The Concept of GxP in Pharmaceuticals. https://www.pharmaguideline.com/2017/01/concept-of-gxp-in-pharmaceuticals.html (Accessed 2024-07-27).
199. Shute, R. E. Blockchain, Distributed Ledger Technology and GxP: The Trust Protocol Enhancing Compliance. https://www.linkedin.com/pulse/blockchain-distributed-ledger-technology-gxp-trust-protocol-shute/ (Accessed 2024-07-27).
200. Liu, Y.; He, D.; Obaidat, M. S.; Kumar, N.; Khan, M. K.; Raymond Choo, K.-K. Blockchain-Based Identity Management Systems: A Review. *J. Netw. Comput. Appl.* **2020**, *166*, 102731; https://doi.org/10.1016/j.jnca.2020.102731.
201. Szostek, D. Blockchain and the Law. **2019**; https://doi.org/10.5771/9783845298290.
202. Yafimava, D. Blockchain And The Law: Regulations Around the World. https://openledger.info/insights/blockchain-law-regulations/ (Accessed 2024-07-27).
203. Rose, P. Blockchain and the Law. https://www.blockchainandthelaw.com (Accessed 2024-07-27).
204. Powers, M. How Blockchain Projects Can Succeed (And Avoid Legal Hassles) in the USA. https://cryptobriefing.com/blockchain-legal-usa (Accessed 2024-07-27).
205. Finck, M. *Blockchain Regulation and Governance in Europe*; Cambridge: Cambridge University Press, 2018.
206. EU. Legal and Regulatory Framework for Blockchain. https://digital-strategy.ec.europa.eu/en/policies/regulatory-framework-blockchain (Accessed 2024-07-27).
207. Lawtech. Blockchain: Legal and Regulatory Guidance Report (Third Edition). https://www.lawsociety.org.uk/topics/research/blockchain-legal-and-regulatory-guidance-report (Accessed 2024-07-27).
208. GLI. Blockchain & Cryptocurrency Laws and Regulations 2023 | Japan. https://www.globallegalinsights.com/practice-areas/blockchain-laws-and-regulations/japan (Accessed 2024-07-27).
209. GLI. Blockchain & Cryptocurrency Laws and Regulations 2023 | Canada. https://www.globallegalinsights.com/practice-areas/blockchain-laws-and-regulations/canada (Accessed 2024-07-27).
210. Schaub, M.; Zhou, S.; Hong, D. What the New PRC Blockchain Regulations Mean. https://www.chinalawinsight.com/2019/02/articles/finance/what-the-new-prc-blockchain-regulations-mean (Accessed 2024-07-27).
211. BBVA. 7 Regulatory Challenges Facing Blockchain. https://www.bbva.com/en/7-regulatory-challenges-facing-blockchain (Accessed 2024-07-27).
212. BBVA. EU Markets in Cryptoassets (MiCA) Regulation: What is it and why Does it Matter? https://www.bbva.com/en/innovation/eu-markets-in-cryptoassets-mica-regulation-what-is-it-and-why-does-it-matter/ (Accessed 2024-11-01).
213. Namecoin. Against Censorship. https://www.namecoin.org (Accessed 2024-07-27).
214. Wikipedia. Domain Name System. https://en.wikipedia.org/wiki/Domain_Name_System (Accessed 2024-07-27).
215. Dogecoin Foundation. Dogecoin Project, Dogecoin the People's Cryptocurrency. https://dogecoin.com (Accessed 2024-07-27).
216. Litecoin. Litecoin – The Future of Money. https://litecoin.com (Accessed 2024-07-27).

217. Wikipedia. Turing Completeness. https://en.wikipedia.org/wiki/Turing_completeness (Accessed 2024-07-27).
218. Nibley, B. What Is ERC20? A Guide to the Ethereum Token Standard. https://www.sofi.com/learn/content/what-is-erc20-token-standard (Accessed 2024-07-27).
219. Wikipedia. Initial Coin Offering. https://en.wikipedia.org/wiki/Initial_coin_offering (Accessed 2024-07-27).
220. Fernando, J. Initial Public Offering (IPO): What it is and how it Works. https://www.investopedia.com/terms/i/ipo.asp (Accessed 2024-07-27).
221. Conti, R.; Schmidt, J. What is an NFT? How do NFTs Work? https://www.forbes.com/advisor/in/investing/cryptocurrency/what-is-an-nft-how-do-nfts-work (Accessed 2024-07-27).
222. Nambiampurath, R. Ethereum Finally Completes The Merge. https://www.investopedia.com/ethereum-completes-the-merge-6666337 (Accessed 2024-07-27).
223. Rhodes, D. What is Delegated Proof of Stake? An Overview of DPoS Blockchains. https://komodoplatform.com/en/academy/delegated-proof-of-stake (Accessed 2024-07-27).
224. Frankenfield, J. Proof of Burn (Cryptocurrency). https://www.investopedia.com/terms/p/proof-burn-cryptocurrency.asp (Accessed 2024-07-27).
225. Zheng, X.; Feng, W. Research on Practical Byzantine Fault Tolerant Consensus Algorithm Based on Blockchain. *J. Phys.: Conf. Ser.* **2021**, *1802*, 032022; https://doi.org/10.1088/1742-6596/1802/3/032022.
226. Hooda, P. Practical Byzantine Fault Tolerance (pBFT). https://www.geeksforgeeks.org/practical-byzantine-fault-tolerancepbft (Accessed 2024-07-27).
227. Neo, Resilience, Meet Innovation. https://neo.org (Accessed 2024-07-27).
228. Ledger.com. Transactions Per Second (TPS) Meaning. https://www.ledger.com/academy/glossary/transactions-per-second-tps (Accessed 2024-07-27).
229. ICON. Go Cross-Chain with ICON. https://icon.community (Accessed 2024-07-27).
230. Dodds, R. Delegated Proof of Contribution. https://medium.com/@ricky_96150/delegated-proof-of-contribution-40bfac995c1 (Accessed 2024-07-27).
231. Rampen, J. New Release: Hyperledger Fabric 2.2 LTS. https://www.hyperledger.org/blog/2020/07/20/new-release-hyperledger-fabric-2-2-lts (Accessed 2024-07-27).
232. Business APAC. A Sneak Peek Into The Evolution Of Blockchain. https://www.businessapac.com/sneak-peek-evolution-of-blockchain (Accessed 2024-07-27).
233. Wikipedia. Directed Acyclic Graph. https://en.wikipedia.org/wiki/Directed_acyclic_graph (Accessed 2024-07-27).
234. Sanders, W. How Directed Acyclic Graphs (DAGs) Solve the Problem of Forking. https://beincrypto.com/learn/directed-acyclic-graphs (Accessed 2024-07-27).
235. Thake, M. What is DAG Distributed Ledger Technology? https://maxthake.medium.com/what-is-dag-distributed-ledger-technology-8b182a858e19 (Accessed 2024-07-27).
236. Wikipedia. OTA (technology). https://en.wikipedia.org/wiki/IOTA_(technology) (Accessed 2024-07-27).
237. Chen, F.; Li, H.; Sui, Z.; Liu, K.; Tang, W. Fast Probabilistic Consensus Protocol (FPC) Under Different Network Topologies. In *2022 International Conference on Service Science (ICSS)*, 2022; pp. 57–63.
238. Wikipedia. Hashgraph. https://en.wikipedia.org/wiki/Hashgraph (Accessed 2024-07-27).
239. Hedera. Hedera Hashgraph. https://hedera.com/learning/hedera-hashgraph (Accessed 2024-07-27).
240. Hedera. HBAR (ℏ). https://hedera.com/hbar (Accessed 2024-07-27).
241. Nano. Nano is a Digital Currency for Everyone, Without Fees. https://nano.org (Accessed 2024-07-27).
242. Obyte. A Ledger Without Middlemen. https://obyte.org (Accessed 2024-07-27).
243. Cardano. Making the World Work Better for All. https://cardano.org (Accessed 2024-07-27).
244. Cardano. What is Ada? https://cardano.org/what-is-ada (Accessed 2024-07-27).
245. Gudgeon, L.; Moreno-Sanchez, P.; Roos, S.; McCorry, P.; Gervais, A. In *Financial Cryptography and Data Security*, 2020; pp. 201–226.
246. Wikipedia. Lightning Network. https://en.wikipedia.org/wiki/Lightning_Network (Accessed 2024-07-27).
247. Smith, C. Plasma Chains. https://Ethereum.org/en/developers/docs/scaling/plasma (Accessed 2024-07-27).
248. Poon, J.; Buterin, V. Scalable Autonomous Smart Contracts. https://plasma.io/plasma.pdf (Accessed 2024-07-27).
249. Wikipedia. Polygon (blockchain). https://en.wikipedia.org/wiki/Polygon_(blockchain (Accessed 2024-07-27).
250. Blockchain Council. What is Cosmos? A Beginner's Guide. https://www.blockchain-council.org/blockchain/what-is-cosmos (Accessed 2024-07-27).
251. Hodl_Lord. NEOX? What is it? https://www.reddit.com/r/NEO/comments/72lx2b/neox_what_its_it (Accessed 2024-07-27).
252. Kusama. Parachains are here. https://kusama.network (Accessed 2024-07-27).
253. Yellow Blog. All You Need to Know About Canary Networks & What Duckies, Yellow's Canary Network, Do for Web3. https://medium.com/yellow-blog/all-you-need-to-know-about-canary-networks-what-duckies-yellows-canary-network-do-for-web3-555b66549dfe (Accessed 2024-11-01).
254. Filippo. Parachains. https://wiki.polkadot.network/docs/learn-parachains (Accessed 2024-07-27).
255. Wikipedia. Self-sovereign Identity. https://en.wikipedia.org/wiki/Self-sovereign_identity (Accessed 2024-07-27).
256. Wikipedia. Zero-Knowledge Proof. https://en.wikipedia.org/wiki/Zero-knowledge_proof (Accessed 2024-07-27).
257. Wikipedia. Dash (cryptocurrency). https://en.wikipedia.org/wiki/Dash_(cryptocurrency (Accessed 2024-07-27).

258. Wikipedia. Monero. https://en.wikipedia.org/wiki/Monero (Accessed 2024-07-27).
259. Wikipedia. Zcash. https://en.wikipedia.org/wiki/Zcash (Accessed 2024-07-27).
260. Sovrin Foundation. Sovrin. https://sovrin.org (Accessed 2024-07-27).
261. BigChainDB GmbH. Meet BigchainDB – The Blockchain Database. https://www.bigchaindb.com (Accessed 2024-07-27).
262. Storj Labs. Globally Distributed Cloud Object Storage. https://www.storj.io (Accessed 2024-07-27).
263. Swarm. Storage and Communication for a Sovereign Digital Society. https://ethersphere.github.io/swarm-home (Accessed 2024-07-27).
264. Sia Foundation. Decentralized Data Storage. https://sia.tech (Accessed 2024-07-27).
265. Fluree. Data 3.0. https://flur.ee (Accessed 2024-07-27).
266. NGI ONTOCHAIN. GraphChain: A Framework for On-Chain Data Management for ONTOCHAIN. https://ontochain.ngi.eu/content/graphchain (Accessed 2024-07-27).
267. Sopek, M.; Gradzki, P.; Kosowski, W.; Kuziski, D.; Trójczak, R.; Trypuz, R. GraphChain. In *Companion of the The Web Conference 2018 on The Web Conference 2018 – WWW'18*, 2018; pp. 1171–1178.
268. Block Convey. An Insight Towards the Fourth Generation of Blockchain Solutions. https://www.blockconvey.com/post/an-insight-towards-the-fourth-generation-of-blockchain-solutions (Accessed 2024-07-27).
269. Mukherjee, P.; Pradhan, C. Blockchain 1.0 to Blockchain 4.0—The Evolutionary Transformation of Blockchain Technology. In *Blockchain Technology: Applications and Challenges*; Springer Nature: New York, 2021; pp 29–49.
270. AlgoShare. Five Generations Of Computers & Blockchain. https://medium.com/@AlgoShare/five-generations-of-computers-blockchain-403be90890ce (Accessed 2024-07-27).
271. Salimitari, M.; Joneidi, M.; Chatterjee, M. AI-Enabled Blockchain: An Outlier-Aware Consensus Protocol for Blockchain-Based IoT Networks. In *2019 IEEE Global Communications Conference (GLOBECOM)*, 2019; pp. 1–6.
272. Multiversum. A Relational Blockchain as a Service for Crypto-Relational Database. https://multiversum.io (Accessed 2024-07-27).
273. Monti, M. Multiversum: 4th Generation Blockchain. https://medium.com/@matteo.monti/multiversum-4th-generation-blockchain-1e1b7b286ec1 (Accessed 2024-07-27).
274. Wikipedia. Shard (Database Architecture). https://en.wikipedia.org/wiki/Shard_(database_architecture (Accessed 2024-07-27).
275. Hydrus7 Labs. The Fourth-Generation Blockchain Technology Leading us to a Sustainable and Better Future. https://www.hydrus7.org (Accessed 2024-07-27).
276. Sovereignwallet. MetaMUI Internet of Sovereign Digital Currencies. https://sovereignwallet.network (Accessed 2024-07-27).
277. Frikken, K. B. Secure Multiparty Computation (SMC). In *Encyclopedia of Cryptography and Security*; Springer Nature: New York, 2011; pp 1121–1123.
278. Grumbling, Emily; Horowitz, Mark *Quantum Computing: Progress and Prospects*; Grumbling, Emily, Horowitz, Mark, Eds.; National Academic Press: Washington, DC, 2019. https://nap.nationalacademies.org/read/25196/chapter/1 (accessed February 13, 2025).
279. Wikipedia. Shor's Algorithm. https://en.wikipedia.org/wiki/Shor%27s_algorithm (Accessed 2024-07-27).
280. Chen, L.; Jordan, S.; Liu, Y.-K.; Moody, D.; Peralta, R.; Perlner, R.; Smith-Tone, D., 2016. Report on Post-Quantum Cryptography. https://doi.org/10.6028/nist.Ir.8105 (Accessed 2024-07-27).
281. Wikipedia. Post-Quantum Cryptography. https://en.wikipedia.org/wiki/Post-quantum_cryptography (Accessed 2024-07-27).
282. Bennett, C. H.; Brassard, G.; Ekert, A. K. Quantum Cryptography. *Sci. Am.* **1992**, *267*, 50–57; https://doi.org/10.1038/scientificamerican1092-50.
283. Wikipedia. Quantum Key Distribution. https://en.wikipedia.org/wiki/Quantum_key_distribution (Accessed 2024-07-27).
284. NCSC. Quantum Security Technologies. https://www.ncsc.gov.uk/whitepaper/quantum-security-technologies (Accessed 2024-07-27).
285. Fedorov, A. K.; Kiktenko, E. O.; Lvovsky, A. I. Quantum Computers Put Blockchain Security at Risk. *Nature* **2018**, *563*, 465–467; https://doi.org/10.1038/d41586-018-07449-z.
286. Collector, Q. R. Quantum Resistant Blockchain and Cryptocurrency, the Full Analysis in Seven Parts. Part 1. https://medium.com/the-capital/quantum-resistant-blockchain-and-cryptocurrency-the-full-analysis-in-seven-parts-part-1-daa211565a68 (Accessed 2024-07-27).
287. Fernandez-Carames, T. M.; Fraga-Lamas, P. Towards Post-Quantum Blockchain: A Review on Blockchain Cryptography Resistant to Quantum Computing Attacks. *IEEE Access* **2020**, *8*, 21091–21116; https://doi.org/10.1109/access.2020.2968985.
288. Bashir, I. *Blockchain Consensus* **2022**; https://doi.org/10.1007/978-1-4842-8179-6.
289. QRL. The Quantum Resistant Ledger. https://www.theqrl.org (Accessed 2024-07-27).
290. XX network. Frequently Asked Questions About the xx Network. https://xx.network/faq (Accessed 2024-07-27).
291. QANplatform. Game-changing Layer 1. Code in any Language. Resist Quantum-attacks. https://www.qanplatform.com (Accessed 2024-07-27).
292. QBI. Quantum Blockchains: Increasing the Security of Blockchains, Accelerating the Adoption of Quantum Cryptography. https://quantumblockchains.io (Accessed 2024-07-27).
293. QBI. Quantum Blockchains: Our Papers. https://quantumblockchains.io/our-papers/ (Accessed 2024-07-27).
294. Misiaszek-Schreyner, M.; Kujawski, Ł.; Kosik, M.; Kulicki, P.; Sopek, M. Introducing Quantum Secured Blockchain: A Comprehensive Whitepaper. https://www.quantumblockchains.io/decks/QSB_whitepaper.pdf (Accessed 2024-07-27).
295. Wikipedia. Internet of Things. https://www.wikipedia.org/wiki/Internet_of_things (Accessed 2024-07-27).
296. BBA. UK's National Blockchain Roadmap (NBR). https://britishblockchainassociation.org/national-blockchain-roadmap-vision-2030 (Accessed 2024-07-27).

297. APO. The National Blockchain Roadmap: Progressing Towards a Blockchain-Empowered Future. https://apo.org.au/node/276541 (Accessed 2024-07-27).
298. Matheson, L. Canadian Lawmakers Back Blockchain with Landmark Recommendations. https://www.coinbase.com/blog/canadian-lawmakers-back-blockchain-with-landmark-recommendations (Accessed 2024-07-27).
299. Tynmagazine.com. Blockchain's Evolution and Enterprise Use Cases, and the Hunt for the Killer App. https://tynmagazine.com/blockchains-evolution-and-enterprise-use-cases-and-the-hunt-for-the-killer-app/ (Accessed 2024-07-27).
300. CB Information Services, How Amazon, Microsoft, and Google are Supporting Web3 and Blockchain Development. https://www.cbinsights.com/research/amazon-microsoft-google-web3-blockchain-developments/ (Accessed 2024-07-27).
301. Munro, A. Ethereum 2.0: Roadmap, Timeline and Implications. https://www.finder.com.au/ethereum-2-0-roadmap-timeline-and-implications (Accessed 2024-07-27).
302. Ashmore, D. A Brief History Of Web 3.0. https://www.forbes.com/advisor/investing/cryptocurrency/what-is-web-3-0 (Accessed 2024-07-27).
303. Paradigm Research. Decentralized Science (DeSci): Web3-Mediated Future of Science. https://medium.com/paradigm-research/decentralized-science-desci-web3-mediated-future-of-science-2547f9a88c40 (Accessed 2024-11-01).
304. Accenture. AI & Blockchain: Chemical Industry Insights and Actions. https://www.accenture.com/us-en/insights/chemicals/ai-blockchain-chemical-industry (Accessed 2024-07-27).
305. Wikipedia. The Salmon of Doubt. https://en.wikipedia.org/wiki/The_Salmon_of_Doubt (Accessed 2024-07-27).
306. Wikipedia. Roy Amara. https://en.wikipedia.org/wiki/Roy_Amara (Accessed 2024-07-27).
307. The Best Universities for Blockchain in the World, updated in February 2024 by EduRank. https://edurank.org/cs/cryptography (Accessed 2024-07-27).