AI 4 Science Discovery Network+

AI4SD Interview with Dr Al Dossetter
30/11/2021
Online Interview

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Network: Artificial Intelligence and Augmented Intelligence for Automated Investigations for Scientific Discovery

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Title	AI4SD Interview with Dr Al Dossetter
Interviewer	MP: Michelle Pauli - MichellePauli Ltd
Interviewee	AD: Dr Al Dossetter - MedChemica Ltd
Interview Location	Online Interview
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2 Biography

Figure 1: Dr Al Dossetter

Dr Al Dossetter: 'The computers won't replace you, but the chemists that use them will replace the chemists that don't'

Al Dossetter is the co-founder of MedChemica, which is centred around the technology of Matched Molecular Pair Analysis (MMPA) as a method of accelerating medicinal chemistry. MedChemica now licenses a suite of artificial intelligence software and databases for organisations to extract and share knowledge from their own data. The software and methodologies have been used by chemists in many pharmaceutical companies, universities and bio-techs to accelerate drug discovery programmes. Previous to MedChemica Al gained his PhD from Nottingham University and after post-doctoral research at Harvard University joined AstraZeneca.

In this Humans of AI4SD interview he discusses whether the rules of medicinal chemistry actually work, achieving 'sensible AI', and the importance of being able to learn quickly.

3 Interview

MP: What's been your path to where you are today?

AD: Back when I was a teenager, I really liked technology and computers — I even used to programme eight-bit computers. When I was doing my A-levels, I got into chemistry, and went on to do a degree at university. After this, I went straight on to a PhD in chemistry at the University of Nottingham, then I did the classic next step: a postdoc in the States. If you did your postdoc then, it was easier to get a job, and a higher salary, once you went into industry. It was a travelling postdoc funding by GlaxoSmithKline (GSK), which meant I could choose where I wanted to go in the States. I really wanted to work at Harvard, so I did 18 months there, which was fantastic.

When I came back to the UK, I was torn between wanting to become an academic and wanting to go into industry. I'm also a rock climber, so I had to be in the north of England otherwise it would've been a miserable life! So I got lucky and had the convenience of working at Alderley Park, where I signed a contract first with Zeneca, which then became AstraZeneca. That meant that I was on the edge of the Peak District which is one of the best places to climb!

MP: What kind of work did you do with AstraZeneca and how did it lead to what you do today?

AD: I was a medical chemist, which meant I could take my knowledge from organic chemistry to design drugs. I worked initially in oncology, then I did inflammation, which was both osteoarthritis and rheumatoid arthritis. Then I moved into the cardiovascular area, working on diabetes and obesity research. In all of this work, people kept saying to me, "These are the rules of medicinal chemistry," but they never entirely worked. So in the mid-noughties, I decided to find out whether one, just one, medicinal chemistry rule actually worked. I spent days on it, and when I actually got the data, I discovered that this rule only worked 8% of the time. Not only that, 11% of the time, it actually made things significantly worse! When I first presented these results in the hallowed halls of AstraZeneca — where Imperial Chemical Industries [ICI] had been, where beta blockers were discovered — they might as well have nailed me to a tree and burned me as a heretic! For the first few years doing this, everyone was saying, "You've done your analysis wrong. Everybody knows this works," despite the fact that I had 2,000 examples of it. So that's where I started my journey of researching whether rules of medicinal chemistry actually worked.

Two colleagues who are now my business partners, Ed and Andrew, were also interested in doing this. We started trying to build a knowledge system, which would automatically trawl through data to make discoveries. That's how Andrew invented the system's modus operandi, Match Molecular Pair Analysis, which is the phrase we coined. It's taken us, years and only in the last couple, before this became part of medicinal chemistry lexicon.

The problem with doing this work at AstraZeneca was that it had to be done in our spare time, which meant that it never really got finished. So we decided to leave and start our own company to do it properly. This was before everybody went AI crazy — we didn't even call it AI, we called it knowledge-based systems. We'd been working at it for five years before people started talking about creating AI companies, and we were saying, "We've got it here!". We could use the technology to share knowledge between large pharmaceutical companies. We already knew in 2012 that there wasn't enough data, you need a diversity of chemical data and that's what we're out to get.

We started to do some big talks, where people responded with "That's stupid", "Why are you doing that?" "You'll go out of business," and I'd sit there saying "We've already done it! We've already shared the knowledge. This is real data." Wow, talk about pushing the rock up the hill! One time we were invited to give a talk and the response was "This isn't AI. AI equals machine learning, and you're not using something like a deep learning neural net." But we didn't need to use machine learning, we could just count how many times stuff works, it's as simple as that. Now, we actually supply our software to two of the large companies that do AI at their core. They don't call us stupid or silly any more, but it's been a heck of a journey to get here!

MP: Why was there so much hostility and resistance to you?

AD: It's the same in a lot of industries: people are worried that these discoveries are going to cost them their jobs. Between 2006 and 2015, large pharma was downsizing and people were being made redundant, so they didn't like the idea of having a computer system outperform them. But the way we sell it is to clarify that this isn't full level-five artificial intelligence, it's not even level four or three, it's a type of augmentation. You still have to use your nous to do it. The younger people have more of a willingness to learn about it, but if you've been doing it for 20 years, you don't want the machine to show your inadequacies.

I have been at conferences with people poking me in the chest saying "You will never replace me. I'm an expert. No computer can do what I do." And I don't argue with that — computers and humans are different. All we can do is explain how we've done the analysis, and what the computer has found and often, what you thought you knew doesn't hold true. The computers won't replace you, but the chemists that use them will replace the chemists that don't. We've witnessed firsthand the computational chemists coming out of pharma and going to the companies that do this, because they're getting fed up with the resistance to it. When large companies in industry have spectacular failures, all that people at the top of the company can do is to close a department, and everybody loses their job. But if you get there more quickly and more cheaply, and you can with AI tools, it means you fail more quickly, and it doesn't cost anybody their job. So, you've got to embrace these tools, otherwise they'll just licence the compounds from BenevolentAI or outsource projects to Exscientia.

MP: Where do you see yourself going in the long term?

AD: What we've achieved is "sensible AI", to quote one of our customers, and with that, a curious thing occurs. You wouldn't call the sat-nav in your car an AI system, but to somebody in the 80s, that's an AI system. AI seems to be this elusive thing that doesn't exist once you've accepted it into your life. Because more people are recognising that Match Molecular Pair Analysis is something sensible, something you need to have, that means we're going to be a sustainable business, but now that means it is not AI anymore.

In terms of the future of AI, we're still experiencing the lack of diversity in the data. It looks voluminous, but there's still not enough. People are working with us to discover where they're deficient in data, and that's the next step. Take, for example, self-driving cars. They're very good at driving into shop fronts because they can't tell the difference between going into a shop front and going under a bridge. If you've ever done the "I am not a robot" test on a website, where you're identifying fire hydrants or traffic lights, you're working for Google; you're gathering the dataset they need for autonomous vehicles. The vehicles, the mechanics, and the computer program are fine, but the dataset to process visuals correctly is not diverse enough. So there's a footrace at the moment around who can diversify their data the fastest.

We have a set of software for identifying the gaps in the chemistry, select compounds to go and test. If we had several million quid, we'd go off and test the compounds and make our database the best there is. It already is the best database there is! That's the arrogant salesman in me!

MP: What advice would you give to early career researchers?

AD: When you ask astronauts "What's NASA after in pilots?" they say, "The ability to learn, to find lots of things interesting, to take new stuff on board, to have a diverse range of experience and knowledge." For young people, the future is being Jacks and Jills of many trades. Don't close your mind to taking on different techniques to achieve a task. Lots of people have great maths skills, others have great chemistry skills, and others have great physics skills. The innovations come when people put these things together. If you have that ability to learn things quickly, if you want to put the effort in to learn the techniques, then it might be worth the investment. We profiled a lot of chemists once, and their highest skill was the ability to learn really quickly. You can't thrive in the drug discovery world without it.