



Artificial Intelligence and Augmented Intelligence for Automated Investigations for Scientific Discovery

AI3SD Interview with Professor Matthew Todd
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Professor Matthew Todd, Professor of Drug Discovery, UCL, takes the AI3SD Q+A.

1 Interview Details

Title	AI3SD Interview with Professor Matthew Todd
Interviewer	MP: Michelle Pauli - MichellePauli Ltd
Interviewee	MT: Professor Matthew Todd - University College London
Interview Location	AI3SD Conference 2019
Dates	18/11/2019

2 Biography



Figure 1: Professor Matthew Todd

Mat Todd was born in Manchester, England. He obtained his PhD in organic chemistry from Cambridge University in 1999, was a Wellcome Trust postdoc at The University of California, Berkeley, a college fellow back at Cambridge University, a lecturer at Queen Mary, University of London and between 2005 and 2018 was at the School of Chemistry, The University of Sydney. He is now Chair of Drug Discovery at University College London. He lives in Greenwich, London, with his wife and two children. Mat's research interests include the development of new ways to make molecules, particularly how to make chiral molecules with new catalysts. He is also interested in making metal complexes that do unusual things when they meet biological molecules or metal ions. His lab motto is "To make the right molecule in the right place at the right time", and his students are currently trying to work out what this means. He has a significant interest in open science, and how it may be used to accelerate research, with particular emphasis on open source discovery of new medicines. He founded and currently leads the Open Source Malaria (OSM) and Open Source Mycetoma (MycetOS) consortia, and is a founder of a broader Open Source Pharma movement. He is on the Editorial Boards of PLoS One, ChemistryOpen and Nature Scientific Reports.

3 Interview

MP: Your AI3SD-funded project is titled *Predicting the activity of drug candidates where there is no target*. In a nutshell, what is it?

MT: We host a consortium called Open-Source Malaria (OSM), where we’re trying to find new medicines for malaria in an open-source, inclusive way, drawing on advances in artificial intelligence (AI) and machine learning (ML). Not a vaccine but medicines to treat people who have malaria – simple medicines that are designed to be inexpensive. There are already medicines but we always need new ones because resistance emerges and you need a pipeline of treatments coming through.

MP: What’s the challenge in creating new malaria treatments?

MT: Frequently, you are faced with a situation where you have a really good molecule that’s killing the malaria parasite, but you don’t know how the molecule is doing it. It’s very common in drug discovery, and is called “phenotypic” drug discovery – drug kills bug, you don’t know how. Finding out how it’s doing it is quite hard, yet making changes to the molecule and measuring whether it’s better or worse at killing the parasite is quite easy, so you do the work to make the molecule better and better but you can’t improve the drug rationally. You can’t be logical about spotting what it’s doing in detail and make little changes to make that better, because you don’t have a molecular target yet, basically. Instead, you have suspicions and you make educated guesses, based on your experience, the community’s experiences, intuition.

What we found over the years is that, as you get more and more into the project and you start making single atom changes to your molecules, even at a late stage you can accidentally obliterate the desired properties and make molecules that don’t work. To some extent that’s useful but it’s also a waste of money. It’d be great to not spend time and money making molecules that don’t work.

MP: And how does that become your AI3SD-funded project in OSM?

MT: Suppose in a project you’ve made up 300 molecules and there’s a range of potencies against the parasites. Some are very potent, some middling, some are not potent at all. So you look at those structures on a piece of paper and a medicinal chemist will have a sense of, “Okay, well based on all of that, I think I know what I need to do.” But it’s quite hard, because you’ve got to look at 300 molecules. We’ve always thought how good it would be if we could get better at predicting things, better computation, better algorithms to look at the data, spot the patterns. We’ve tried over the years, with fairly basic technologies that were around four or five years ago but it didn’t work very well.

A couple of years ago, we invited people to have a look at all of our data and be predictive about what we needed, and it went well. A good example of the hive mind. We had six entries from around the world and they all used different methods but the models they came up with weren’t terribly predictive, or at least not as predictive as we needed them to be if we were going to use the models to make potent molecules.

However, in the intervening two or three years, AI and machine learning have become a big deal. So we thought, “Ok, let’s run it again.” And that’s what the AI3SD funding has enabled us to do. We have invited companies and individuals again to take part in a predictive

modelling competition, this time deploying AI and ML technologies. We’ve received 10 entries, from amateurs and leading AI companies, and about half from companies who participated before. We’re asking those who win the competition – the best predictive models – to use the technologies to predict new molecules, that have never existed before, and we’re going to make them, then measure how effective they are at killing the parasite in blood.

MP: What part does the open source aspect play?

MT: All our data was already shared: everyone could see what was involved, play with everything, see each other’s entries, see what each other was doing in real time, and take note or not, as they wish. At one point, one of the competition entrants posted a different version of our data spreadsheet that was better than ours because he’d rearranged everything so that other people could then use the data better.

We shared all the data on a Google sheet, we had a discussion online using GitHub and we tweeted to try and make people aware of what was going on. But we didn’t prescribe what tools people should use for the AI aspect, because some people used freely available tools and the companies used their own proprietary magic.

MP: Has anything surprised you?

MT: The competition was intentionally a little bit vague because we wanted people to do whatever they wanted. As a result, the data came in from different people in different ways and we had to find a way of comparing the data fairly. We were surprised at how much better the models were this time. That may be partly because the data are a bit more focused on our molecules whereas the data previously were quite general, quite diverse structures, but that’s fine. Either way, we’re surprised at how good the models now are, which means the predictions should be active when we make them and I’m hoping that we’ll have a nice case study of usefulness.

MP: More generally, is AI or ML changing how we do science?

MT: For sure, it is. As an example, for many years it was thought that the design of how to make complicated molecules over many steps – organic synthesis – was a uniquely human thing. A bit like chess, it was so big and complicated and relied on so many rules of thumb and nuance and years of training and learning, it was like an art form : humans could do it and machines couldn’t.

Then chess was done and it’s obvious that organic synthesis will go the same way. The investment level hasn’t been very high but now it’s happening and there are people who are doing beautiful things with AI to help you plan how to make molecules. Even the hardcore element in chemistry and biology are beginning to think, “Well actually, we need to take notice of it.”

Hopefully, what’s happening is that people are framing it as though AI and ML techniques are allies, that we can move with those tools to make work better, rather than feel threatened by them. I think the fear that we’re somehow being replaced by AI is fundamentally mistaken.

MP: What promise does AI hold for the future?

MT: Children are still dying of malaria at the rate of two full 747s crashing every day. You

don't see it, it's not in the headlines, but it's an absurd number of people dying. The treatment regimens for tuberculosis last 18 months, with some horrific combination of medicines. Every single infectious disease suffers from the problem of resistance. It's not simply a case of having a disease and coming up with a molecule: you have to come up with a continuous stream of molecules very quickly, and have them in reserve. To get to a pace of discovery where we respond quickly to an infectious threat, we need all the help we can get. If you imagine drug discovery becoming 10 times more efficient, people might think the problem's solved. It's not at all. It just means that maybe we might have a chance to keep up with nature a little bit and defeat some of these things.

For me, AI and ML are a way of speeding that up. It's not just about doing it more quickly, it's about changing the way you're doing it, by getting all the help you can.