BIOLOGICAL INTELLIGENCE AND THE BRAINCURES DISCOVERY ENGINE **KRZYSZTOF POTEMPA**

Krzysztof Potempa
Neuroscientist, Founder and Director of BRAINCURES

Krzysztof Potempa is Founder and Director at BRAINCURES. He is a passionate computational neuroscientist with over 10 years of experience in deciphering biology from big data in academia and industry. In August 2016, he established BRAINCURES, to enable streamlined precision medicine based on a novel molecular framework for learning and memory. Their unique biological intelligence approach to de-risk and accelerate drug discovery has been recognized with the Beanstalks 2017 Best Mental Health Startup Award.

Biological intelligence is a proven way to increase success in drug discovery

Biological intelligence is a key ingredient to increasing success in today's drug discovery era. For example, Astra Zeneca has implemented a 5R Framework to improve R&D success rates over the last decade based on right- target, tissue, safety, patient, and commercial potential metrics. These parameters have quadrupled Astra Zeneca's drug development success rate. Similarly, while artificial intelligence (AI) sounds promising, this approach is only learning how to find the needles in the haystacks of data. Thus, based on early successes of molecular stratification in autoimmune diseases, further advances in our understanding of disease biology at the molecular level across most domains will be needed to advance streamlined drug-patient matching for precision medicine.

Biological intelligence requires the discovery of missing molecular links

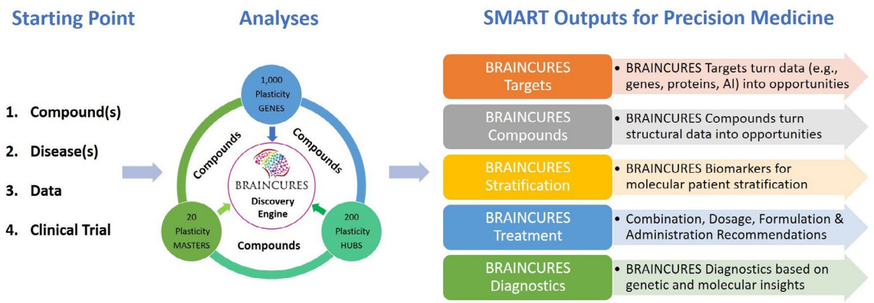
Today one of our greatest challenges on the road to precision medicine is to understand the biology behind how healthy states transition to diseased states and vice versa. To address this knowledge gap, we set out to decode the molecular program behind learning and memory by mapping the genes implicated in memory formation over several different time-points. We then modeled the hundreds of plasticity genes identified with network- and proprietary-analyses. Our iterative and integrative approach allowed us to decipher how the hundreds of mapped plasticity genes interact with each other to form a molecular orchestra comprised of genes, hubs and masters. Furthermore, this orchestra is modulated by several compounds, which we know are powerful tools for disease prevention and management based on retrospective analysis of preclinical and clinical data. This biological intelligence powers the BRAINCURES Discovery Engine.

BRAINCURES Discovery Engine: A Molecular GPS to preclinical and clinical success

The BRAINCURES Discovery Engine enables better, safer and faster drug discovery from multiple starting points (e.g., compound, disease, data, clinical trial). For instance, querying a compound structure against our Discovery Engine established a compound-BRAINCURES Target linkage. This linkage then allowed us to prioritize 66 of the 25 thousand repurposing opportunities generated by a machine learning approach. These opportunities across brain and non-brain disorders were then validated with SMART Literature searches to establish that about a third of them have retrospective evidence in support of stratification. Finally, the target linkage allowed us to identify additional compounds that could be explored for personalized treatments for the identified disease opportunities. Consequently, our unique biological intelligence approach, not only turns outputs from an artificial intelligence approach into actionable insights, but also enables a powerful in silico approach to pipeline management through biology-based prioritization and stratification of assets to increase preclinical and clinical success ■

Applications of the BRAINCURES Discovery Engine

BRAINCURES



UNLOCKING THE FULL POTENTIAL OF DATA THROUGH ADVANCED ANALYTICS **JIM WEATHERALL**

Jim Weatherall,
Vice President of Advanced Analytics and Head of the Advanced Analytics Centre, AstraZeneca

Jim is Vice President of Advanced Analytics and Head of the Advanced Analytics Centre in Global Medicines Development at AstraZeneca, a diverse and global group focussed on their mission of "transforming the development of medicines through applied data science". He is committed to driving the application of advanced analytics as a way of unlocking the full potential of data – through data & text mining, machine learning & artificial intelligence, visual analytics, modelling & simulation, advanced statistical methods, and exploration of new technologies. Jim is an Honorary Reader in Computer Science at the University of Manchester, and Vice-Chair of the Data Science Section at the Royal Statistical Society.

What are your views on the role that machine learning will play in the future of drug discovery?

Machine learning has the potential to play a significant role in the future of drug discovery. This is because drug discovery is a data-intensive endeavour, and the volumes and types of data are now reaching levels of size and complexity where only computers and algorithms are going to be able to identify novel patterns and hypotheses. The idea of using generative-adversarial neural networks for molecular design is exciting, and a number of organisations are currently exploring this approach – essentially taking a positive step towards machine-driven design rather than brute force approaches requiring a physical laboratory, such as high-throughput screening. Furthermore, machine learning is well positioned to infer predictive models from large and diverse data sets – enabling more robust decision making about which molecules to take forward. Imagine if you were able – with a certain degree of accuracy and uncertainty – to confidently predict the clinical efficacy and safety of your medicine, before it ever makes it in to clinical trials. This is an area of huge potential, albeit with some hard work ahead to get the data in shape, and to understand what these complex pattern recognition techniques are really telling us.

In your opinion, what have been the most important developments in AI over the last 12 months?

Firstly, we've seen more organisations embrace the AI branding and create job roles and departments that reflect this, moving past the hype and replacing scepticism with action. Secondly there have been a proliferation of exemplar cases of how these techniques could transform research and development – the aforementioned molecular design using neural networks, being one of these. Thirdly, there have been a number of reports from significant organisations – for example the UK House of Lords released its report "AI in the UK: ready, willing and able?", and Parliament now even has a select committee on AI. And finally, these reports and other sources have significantly advanced the conversation regarding data ethics and algorithmic responsibility.

What are the biggest challenges in integrating AI approaches into a drug development pipeline?

Data and behaviours. These are the two critical success factors for AI to really make a difference. Firstly, data has to be of adequately high volume and quality, otherwise even the most sophisticated AI algorithm will not be able to extract value from it. For behaviours, we are ultimately relying on human beings to make the final call, based on the outputs of AI and machine learning. In order for this to occur, we have to treat AI as much as a 'human problem' as a 'machine problem'. That is, we are trying to understand how best people can interact with AI, what will lead them to trust the outputs, and how to effectively blend their own soft subjective judgement with the outputs of a hard mathematical engine.

Outside of drug discovery, how could AI have an impact on the wider healthcare industry?

There are numerous ways in which AI could have an impact on the wider healthcare industry. We have already seen chat bots and virtual assistants, with whom you can have a 'conversation', in order to discuss your health or medical issues. Then when you enter a clinic or hospital, you could be greeted by a robot who helps to direct you. When you see your doctor, they should be increasingly using the output of AI algorithms to discuss the risk and benefit of various treatments and other interventions with you. And smart devices, sensors, and wearables will be providing a 'closed feedback loop' to keep you continuously abreast of your health status, so that you can take immediate action if required ■

Jim Weatherall will be presenting at the 2nd Annual Artificial Intelligence in Drug Development Congress this September in London as part of our PharmaTec Series with his talk *'The Role Of AI In The Development Of Medicines: Today And Tomorrow'*