Managing the Complexity of Molecules: Letting Matter Compute Itself

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Person-millenia are spent each year seeking useful molecules for medicine, food, agriculture and other uses. For biomolecules, the near infinite universe of possibilities is staggering and humbling. As an example, antibodies, which make up the majority of the top-grossing medicines today, are comprised of 1,100 amino acids chosen from the twenty used by living things. The binding part (variable region) that allows the antibody to bind and recognize pathogens, is about 110 amino acids, giving rise to 10^{143} possible combinations. There are only about 10^{80} atoms in the universe, illustrating the intractability of exploring the entire space of possibility. This is just one example…

Presently, machine learning (ML), artificial intelligence (AI), quantum computing, and "big data" are often put forth as the solutions to all problems, particularly by pontificating TED presenters' pitches dripping with hyperbole. Expecting these methods to provide intelligent de novo prediction of molecular structure and function within our lifetimes is utter rubbish. For example, a neural network trained on daily weather patterns in Palo Alto cannot develop an internal model for global weather. In a similar way, finite and reasonable molecular training sets will not magically cause a generalizable model of molecular quantum mechanics to arise within a neural network, no matter how many layers it is endowed with. Regardless of the algorithms chosen, one simply cannot yet ask a computer to "compute" a drug that cures HIV.

With that provocative preface, we turn to the notion of letting matter compute itself. Massive combinatorial libraries can now be intelligently and efficiently mined with appropriate molecular readouts (AKA "the question vector") at ever-increasing throughputs presently surpassing 10^{12} unique molecules in a few hours. Once "matter-in-the-loop" exploration is embraced, AI, ML and other methods can be brought to bear usefully in closed-loop methods to follow veins of opportunity in molecular space. Several examples of mining massive molecular spaces will be presented, including drug discovery, digital pathology, and AI-guided continuous-flow chemical synthesis – all real, all working today.

Greg Kovacs is Chief Technology Officer for SRI International and leads efforts across the Institute to advance SRI's business model of Invent / Apply / Transition by facilitating research opportunities utilizing science, technology and research talent from all divisions. Kovacs previously served as president of SRI Biosciences for two years.

In the 25 years before joining SRI, Kovacs was a Professor of Electrical Engineering, and by courtesy, Medicine, at Stanford University, primarily researching medical devices. In 2003, his team launched the first professional wearable physiologic monitor capable of wireless, clinical-grade cardiac, respiratory, motion, position and oxygen saturation measurements. He co-founded the Bioengineering Department at Stanford in 2002 and has helped develop the core curriculum. He has authored more than 180 scientific publications, a textbook, and has 63 issued patents. He co-founded several startups, including Cepheid, a molecular diagnostics company that develops molecular diagnostic systems, shipping more than 100 million tests, and PhysioWave, developing non-invasive cardiovascular risk assessment. At DARPA, he served as the director of their Microelectronics Technology Office from 2008 - 2010, overseeing investment of approximately $1.6B in electronics and medical technologies. He holds an M.D. degree and a Ph.D. degree in Electrical Engineering from Stanford University, an M.S. degree in Bioengineering from the University of California, Berkeley and a B.A.Sc. degree in Electrical Engineering from the University of British Columbia. He is a Fellow of the IEEE, AIMBE and the Explorer's Club.