AI CONTINUES TO BUILD THE FOUNDATION FOR A REMARKABLE FUTURE IN BIOLOGY

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July 28, 2022, was a historic day in both biology and artificial intelligence (AI). DeepMind, an Alphabet-owned AI research firm, made the structural data on more than 200 million proteins from its AlphaFold tool freely available. This represents data on roughly 1 million species and covers the vast majority of known proteins on Earth.[1]

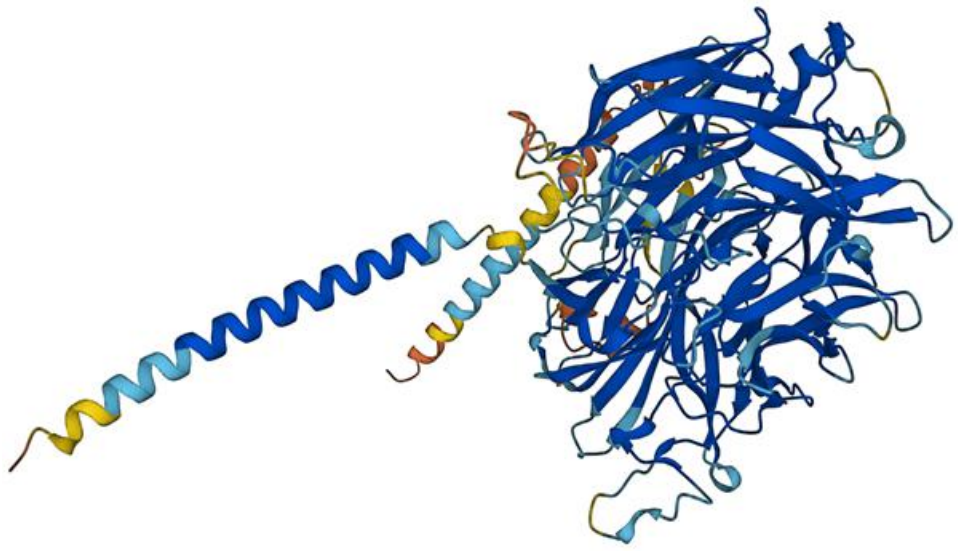
In Proteins, Shape Can Determine Function

In the late 1990s into the early 2000s, the scientific community was awash with news of the race to sequence the human genome. This genome contains the instructions embedded in DNA about how cells should build certain structures, typically by forming proteins made from different combinations of amino acids.

In a sense, DNA is the instruction manual, amino acids are the building blocks and proteins are the product. Knowing the code, though important, is not enough.

Figure 1 is instructive on the point. This is the image of a protein that may protect the organism responsible for malaria from attack by the human immune system. Even if you knew the list and the order of all the amino acids, it would be difficult to go from that list to something that looks like Figure 1 in three dimensions.

Figure 1: Protein Associated with the Malaria Parasite



Source: Alphafold

The importance of the shape of the protein can not be overstated:

- It can correspond to the way in which it might react in the presence of different molecules, like those associated with various drug therapies.

- Variations in the shape—sometimes termed mutations—could be instructive in determining the causal factors of certain symptoms or diseases.
- Parts of the shape could be used as targets. Think of the "spike protein" associated with the virus behind the COVID-19 pandemic, specifically targeted in the mRNA vaccines.

AlphaFold Represents a Leap Forward

Scientific breakthroughs are difficult, in that, in many cases, one builds on another and another and another. The process can take decades before widespread results impact the lives of the general public. For instance, we sequenced the human genome, but that did not necessarily lead to immediate cures for all sorts of diseases or conditions. While mRNA research had been occurring for decades, the COVID-19 pandemic was a catalyst that supercharged the process of using mRNA in the specific case of the vaccines.

AlphaFold's new database is therefore unlikely to lead to immediate cures for challenging conditions. The critical element regards how researchers who would have formerly had to undertake a cumbersome process of X-ray crystallography to determine the shape of a given protein could instead go to the database. Experimental techniques would still have their place, but less time would have to be spent on the equivalent of the blank page.

What's also incredible is that AlphaFold's database is, in conjunction with the European Molecular Biology Laboratory's European Bioinformatics Institute (EMBL-EBI), freely available with a simple interface. It also provides an estimate of the accuracy, recognizing that predictions based on AI do not always yield perfect results. Roughly 35% of the 214 million predictions are deemed highly accurate—roughly as good as experimental results. A further 45% are deemed to be accurate enough for many applications.[2]

Drug Discovery: Better Therapeutics Developed More Efficiently

Even before the onset of inflation at the levels seen in the summer of 2022, it was widely recognized that drug development is time-consuming and expensive. As a result, many medications carry exorbitant price tags. Any process that could mitigate this pressure without degrading the quality of the therapies would be enormously valuable.

Considering the following could be instructive as the space continues to progress:[3]

- **Pipeline Growth:** From 2010 to 2021, 20 smaller companies focused on AI drug discovery, typically with a focus on smaller molecules, had development pipelines that were roughly 50% as robust as those of 20 of the largest big pharma companies. We recognize that the reporting of pipelines may not be perfect and that a molecule in a pipeline is not a finished product, but activity is the first step on the path.
- **Pipeline Composition:** This is not always disclosed, but the information available indicates that AI-focused companies tend to concentrate on well-established biological targets for their therapies, around which much is known. Data is the fuel for AI, and these companies will also want higher chances of success. Bigger pharma companies will be more likely to venture into more emerging areas of drug discovery.
- **Chemical Structures and Properties:** It is too early to draw any robust conclusions regarding AI drug discovery efforts versus big pharma efforts on this point.
- **Discovery Timelines:** Preliminary data appears to indicate that, while traditional approaches tend to take five or six years in preclinical phases, AI-focused drug discovery might be able to, in certain cases, take this timeline down to four years.

We'd note that it's more a story of progress than perfection, in that we appear to be

some distance away from AI being able to fully create new drugs. But AI represents an entirely new set of tools that could have beneficial impacts. AlphaFold's database, for example, may provide drug researchers with important inputs and catalysts for different ideas, even if it doesn't have the immediate answer or cure right there in its system.

Focus on the AI and BioRevolution Megatrends

At WisdomTree, we focus on both the AI megatrend and the BioRevolution megatrend. What we see here with the case of AlphaFold is an important case study in the fact that AI is a tool that can potentially supercharge other megatrends, in this case the BioRevolution. It is no accident that the BioRevolution is ramping up at the same time massive amounts of data, massive amounts of processing power and other things like cloud computing are readily available. It is exciting to consider what the coming decades can bring in these areas.

[1] Source: Callaway, Ewen, "'The Entire Protein Universe': AI Predicts Shape of Nearly Every Known Protein," Nature, Volume 608, 8/4/22.

[2] Source: Callaway, 8/4/22.

[3] Source: Jayatunga et al, "AI in small-molecule drug discovery: a coming wave?" Nature Review: Drug Discovery, Volume 21, 3/22.

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