

Acceptance speech

20 June 2023

David Baker, awardee in the Biology and Biomedicine category (15th edition)

Proteins carry out essentially all of the important functions in our bodies and in all living things. They digest our food, fire our neurons, make molecules in our bodies, and allow us to move.

While the proteins in and around us are incredible, they all evolved to solve problems that were important during natural selection. For example, running away from predators or mediating the thought processes in our brains.

We live in a very different world today. We are living longer, so new conditions like Alzheimer's disease are important. We are heating up and polluting the planet, so we need to find cleaner ways to generate energy and break down plastics and toxic compounds.

We could wait for new proteins to evolve, but this would take many millions of years, and we don't have that kind of time.

To address these new challenges, my colleagues and I have developed methods for designing completely new proteins that can solve new problems. We are using these methods to develop cures for cancer, infectious disease, and more – and new advanced materials and technologies for a more sustainable tomorrow.

The proteins in nature are encoded in the genes in our genomes and those of other living things. Once we have designed a brand new protein, we make a synthetic gene that encodes it (since the protein is new, there is no corresponding gene in nature), and put it into bacteria which then produce the designed protein. We then extract the protein and test it to see if it does what we designed it to do. We have now designed and experimentally tested hundreds of thousands of brand-new proteins that solve a very wide range of

problems. One of these is already a clinically approved medicine; others are on the way.

Proteins are made of thousands of atoms, and we first designed proteins by seeking to accurately model the interactions between these atoms and how they direct the folding of the unique amino acid sequence of a protein to its final 3D structure. In the last several years, we have developed deep learning methods for protein design which are much faster and more accurate. Both our older atomic interaction modeling approach, called Rosetta, and our newer deep learning design methods have been widely adopted around the world.

The progress my team and our many collaborators worldwide have achieved to date has been the result of many hundreds of brilliant minds all working together. To them, I owe my deepest gratitude. This award is as much theirs as it is mine.

To the BBVA Foundation, and everyone present here today, thank you for this honor and for your support. We promise to keep exploring, and to keep sharing, each and every day.