KUNGL. VETENSKAPS-AKADEMIEN
THE ROYAL SWEDISH ACADEMY OF SCIENCES

The Royal Swedish Academy of Sciences has decided to award the Nobel Prize in Chemistry 2024 with one half to **David Baker** "for computational protein design" and the other half jointly to **Demis Hassabis** and **John Jumper** "for protein structure prediction".

The Nobel Prize 2024 **in Chemistry**

They cracked the code for the amazing structures of proteins

The Nobel Prize in Chemistry 2024 is about proteins, life's ingenious chemical tools. David Baker has achieved the almost impossible feat of building new proteins. Demis Hassabis and John Jumper have used an AI model to solve a 50-year-old problem: predicting the complex structures of proteins. These discoveries hold enormous potential.

How is the exuberant chemistry of life possible? The answer to this question is the existence of proteins. These can be described as brilliant chemical constructions. They are generally built from 20 amino acids that can be endlessly combined. Using the information stored in DNA as a blueprint, the amino acids are linked together inside our cells to form long strings.

Then the magic of proteins happens: the string of amino acids twists and folds into a distinct – sometimes unique – three-dimensional structure. This structure is what gives proteins their function. Many proteins control and drive chemical reactions, others function as hormones, signal substances, antibodies or building blocks for various types of tissue.

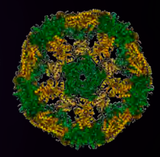
The Nobel Prize in Chemistry 2024 is about understanding and mastering proteins at a completely new level. One half of the prize goes to Demis Hassabis and John Jumper. In 2020 they utilised artificial intelligence to successfully solve the biggest challenge in biochemistry: predicting the three-dimensional structure of a protein from a sequence of amino acids.

The other half of the prize goes to David Baker. He has developed computational methods for achieving what many people believed was impossible: designing entirely new proteins. He created his first protein in 2003. This was the start of extraordinary progress, with his research group developing one spectacular protein after the other.

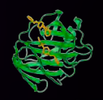
How a protein gets its structure
A protein's three-dimensional structure is decisive for its function, and is formed when the various amino acids begin to interact. Positively and negatively charged amino acids are attracted to each other. Fatty (hydrophobic) amino acids move towards the centre and push away water molecules.

TOP7

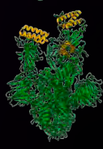
David Baker becomes a protein constructor
Because proteins are such fantastic chemical tools, researchers had long tried to construct ones of their own. Many started from previously existing proteins and tweaked them, but in 2003 David Baker succeeded in building an entirely new protein from scratch. He developed a computer program – Rosetta – that could analyse a desired protein structure and suggest an amino acid sequence for that specific structure. The first protein that David Baker designed, *Top7*, had no similarities to any known protein. After this, David Baker has constructed proteins with a multitude of different functions. A few examples are provided below.



2016: New nanomaterials in which up to 120 proteins spontaneously bind together.

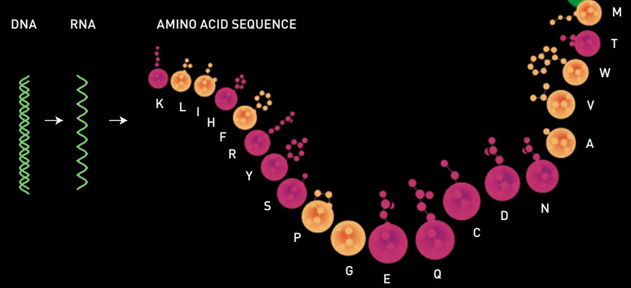


2017: Protein that binds to fentanyl, an opioid (orange). This can be used to detect fentanyl in the environment.



2020: A protein (orange) that can inhibit the virus that causes COVID-19.

From gene to protein
Every gene in our DNA is a description of what a protein should look like. It provides the order – sequence – of the amino acids in a protein. When the cell produces a protein, it copies the description in the DNA to an RNA molecule, which the cell uses as a template when it joins the amino acids into a long string.



Hassabis and Jumper solve the great challenge of biochemistry
For over 50 years, researchers tried to predict the three-dimensional structure of a protein based on knowledge of its amino acid sequence. In 2020, Demis Hassabis and John Jumper solved this problem using an AI model called AlphaFold2.

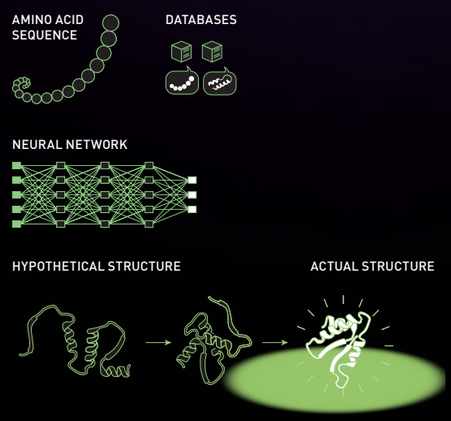
AlphaFold2 has had an enormous impact
Hassabis and Jumper have used AlphaFold2 to predict the structure of all the 200 million now-known proteins. The code for AlphaFold2 has been released, and the AI model has now been used by millions of people around the world.

How does AlphaFold2 work?

1. An amino acid sequence with an unknown protein structure is fed into AlphaFold2. AlphaFold2 searches databases for closely related amino acid sequences and potentially similar protein structures.

2. Using neural networks called transformers, the AI model conducts a deep analysis of all the information it retrieved. This provides insights about which amino acids are likely to be close together in the three-dimensional structure.

3. AlphaFold2 produces a hypothetical structure that it tests and refines over several stages. When the AI model has finished, it has produced a structure that usually corresponds with reality.



David Baker
Born 1962 in Seattle, USA. Professor at University of Washington, Seattle and Investigator, Howard Hughes Medical Institute, USA.

Demis Hassabis
Born 1976 in London, UK. CEO of Google DeepMind, London, UK.

John Jumper
Born 1985 in Little Rock, USA. Senior Research Scientist at Google DeepMind, London, UK.

Photo: Portrait of David Baker: Ian C. Haydon, UW Institute for Protein Design; Portrait of Demis Hassabis: Angela Moore; Portrait of John Jumper: Carolyn Jumper

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More information about the Nobel Prize in Chemistry 2024 is available at *www.kva.se/nobelchemistry2024* and *www.nobelprize.org*, with video and detailed information about the prize and the laureates.

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