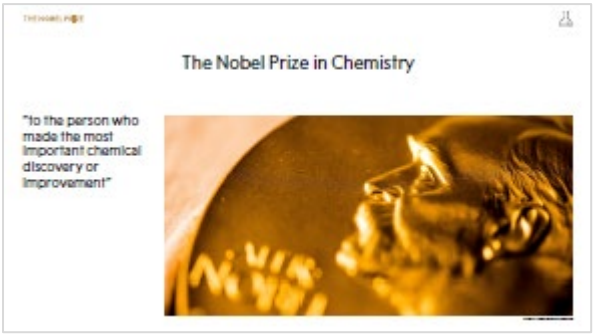
THE NOBEL PRIZE

Speaker's manuscript – Chemistry prize 2024
The secrets of proteins

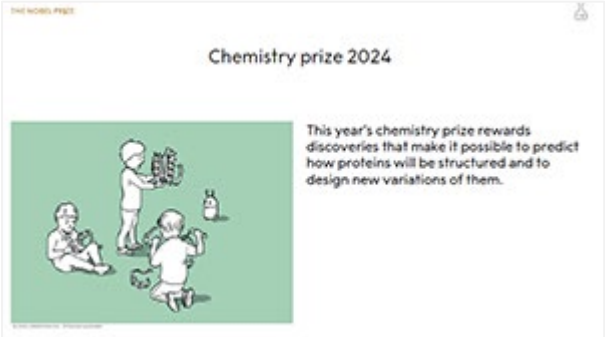
The Nobel Prize in Chemistry



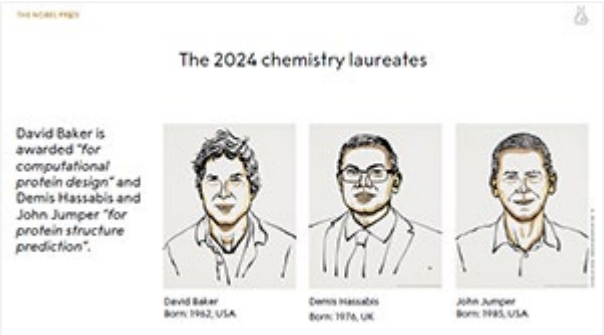
- The Nobel Prize in Chemistry is one of the five prizes founded by the Swedish inventor Alfred Nobel and awarded on 10 December every year.
- Before Alfred Nobel died on 10 December 1896, he wrote in his will that the largest part of his fortune should be placed in a fund. The yearly interest on this fund would pay for a prize given to "those who, during the preceding year, shall have conferred the greatest benefit to humankind."
- The interest would be divided into five equal parts, with one part awarded "to the person who shall have made the most important chemical discovery or improvement".
- The Nobel Prize in Chemistry is thus awarded to people who have made discoveries or improvements that have given us knowledge about the structure of various substances and how they are created and changed.

The 2024 chemistry prize

- The 2024 chemistry prize is about proteins, life's ingenious chemical tools. The laureates have used computers and artificial intelligence (AI) to crack the code for the structures of proteins. These discoveries hold enormous potential.



2024 chemistry laureates

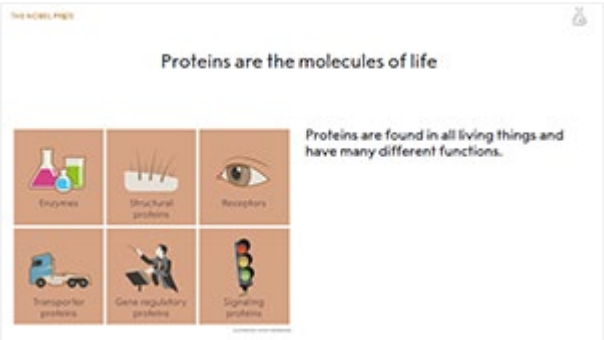


- Half of the prize is awarded to David Baker and the other half jointly to Demis Hassabis and John Jumper.
- David Baker has developed computer-based methods that make it possible to create proteins that did not previously exist and that in many cases have entirely new functions. He works at the University of Washington in the United States.
- Demis Hassabis and John Jumper have used an AI model to predict the structure of essentially all the 200 million proteins known to scientists. Demis Hassabis is the CEO of Google DeepMind in Great Britain. John Jumper is a Senior Research Scientist at Google DeepMind.

What is life?

- In order for something to be classified as living, it must fulfil the following criteria:
  - Maintain a constant internal environment, or homeostasis. For a human, this could mean keeping an even body temperature, a certain salt balance in the body and a certain pH value in the blood.
  - Take in information and react to its surroundings. Humans shiver when we are cold, for example, since this increases friction, which generates heat. Plants turn toward the sun to take in the energy in its light and use it for photosynthesis.
  - Be made up of cells. The cells of multicellular organisms can form tissues, organs and organ systems.
  - Take in and transform nutrients to meet its needs. This is what we mean by metabolism. Plants, animals and single-cell organisms all have metabolism.
  - Reproduce. It can do this asexually, for example through cell division or budding, or sexually.
- None of these criteria can be fulfilled without proteins.

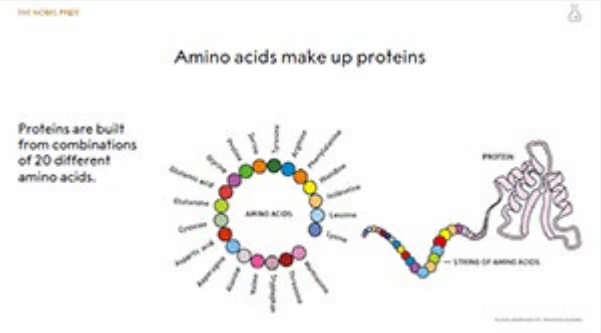
Proteins are the molecules of life



- All living things contain proteins. Proteins can be described as life's ingenious chemical multi-tools.
- Proteins can be divided into different groups according to their functions:

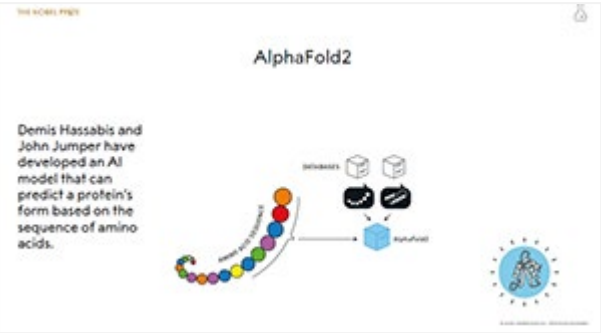
- Structural proteins, with which the structures and tissues of living organisms are built, such as hair, bone and skin.
- Receptor proteins, which take in information from the surrounding environment, such as insulin receptors in the cell membrane.
- Signalling proteins, which process information and pass it on, such as adrenaline.
- Gene regulatory proteins, which control when and how much of a certain protein is synthesised in a cell.
- Transporter proteins, which transport various substances throughout the body with the help of the blood, such as haemoglobin in red blood cells.
- Enzymes, which ensure that chemical reactions in the body occur in an effective way. An example is the chemical reactions that occur in the digestive system.

Amino acids make up proteins



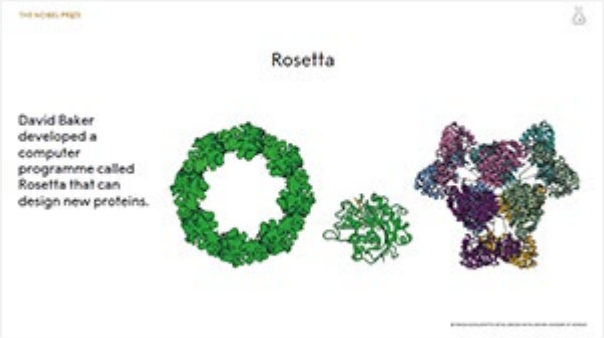
- Proteins are built up of amino acids. These amino acids are linked together like a string of pearls.
- There are 20 different kinds of amino acids that can be linked together in an endless number of different combinations. A protein can be anywhere from about 50 to thousands of amino acids long.
- What makes proteins so amazing is that these strings of pearls twist and fold themselves into specific three-dimensional structures. It is the protein's three-dimensional structure that determines the particular function of each, such as an enzyme.
- For over 50 years, researchers dreamed of being able to predict the three-dimensional structure of a protein, what it looks like, while knowing only the sequence of amino acids.

AlphaFold2



- Demis Hassabis and John Jumper have developed AlphaFold2, an AI model that allows us to predict the structure of a protein if we know the sequence of amino acids.
- In the development of AlphaFold2, they trained the AI model on every known amino acid sequence for which the protein structure had been mapped.
- Now an amino acid sequence with an unknown structure can be fed into AlphaFold2, which searches various databases for similar amino acid sequences with known protein structures.
- What AlphaFold2 does is to puzzle together all these amino acid sequences and tests different ways of assembling them into a hypothetical structure. Then the model estimates the probability that various parts of the structure correspond to reality.

Rosetta

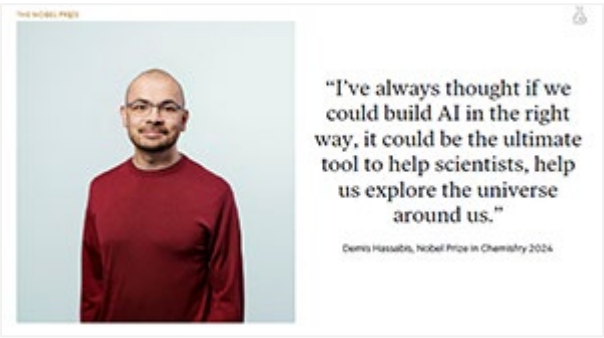


- David Baker began at the other end – that is, he started with a three-dimensional protein structure and figured out its amino acid sequence.
- He and his research group drew up the three-dimensional structure for a hypothetical protein. Then they let the Rosetta programme figure out an amino acid sequence that could produce the desired protein.
- In order to test how successful the programme was, they did the same thing in a laboratory using an established method known as x-ray crystallography.
- It turned out that Rosetta really could construct proteins.
- As a result, today we can start with a sequence of amino acids and create a complete protein, and we can even go in the other direction, from protein structure to amino acid sequence.

For the greatest benefit to humankind

- It used to take many years to determine the structure of a protein, if it could be done at all. Thanks to AlphaFold2, today it can be done in a matter of minutes. The AI model is available for researchers all over the world to use for free. Since the programme was released in 2020, it has been used by more than two million people from 190 countries.
- Knowing a protein's three-dimensional structure makes it possible for researchers to understand various sequences of events in living organisms. That increases our understanding of diseases and paves the way for new pharmaceuticals in the future.
- Equally important is the fact that we now have the ability to design new proteins. With the Rosetta computer programme, researchers can create proteins with new functions – something many once thought impossible.
- Building proteins that are loaded with new functions can give us things like new nanomaterials, targeted pharmaceuticals and faster development of vaccines.

"I've always thought if we could build AI in the right way, it could be the ultimate tool to help scientists, help us explore the universe around us."



- In an interview given in conjunction with the announcement of the 2024 chemistry prize, Demis Hassabis shares his ideas about how AI can be used in research to study the world around us.