On the 2024 Nobel Prize in Chemistry and Its Significance

The 2024 Nobel Prize in Chemistry was awarded to David Baker, Demis Hassabis, and John Jumper for their groundbreaking contributions to the study of protein structures using artificial intelligence and advanced computational techniques. This recognition focuses on two key achievements: the computational design of proteins and the prediction of their three-dimensional structures, both of which have a huge impact on biotechnology and medicine.

David Baker, from the University of Washington, has been a pioneer in designing new proteins through computational algorithms, creating synthetic proteins that can function as drugs, vaccines, and sensors. His work has opened up possibilities for creating customized molecules for specific applications, something unimaginable with traditional methods.

On the other hand, Demis Hassabis and John Jumper from DeepMind (a subsidiary of Google) were awarded for the development of AlphaFold 2, an artificial intelligence system that predicts how proteins fold into their three-dimensional structure based on their amino acid sequence. This breakthrough has solved a problem that had been a challenge for structural biology for decades. AlphaFold 2 has proven capable of predicting models of millions of protein structures, revolutionizing areas such as drug development and disease research.

The Importance of Structural Knowledge of Proteins

Understanding the structure of biological macromolecules is essential because these molecules are fundamental to almost all biological processes. For instance, proteins perform functions like catalyzing chemical reactions (enzymes), regulating cellular processes (hormones), transporting molecules (hemoglobin), and defending the body (antibodies). The three-dimensional structure of a protein determines its function, so to understand how a protein works in an organism and how it can interact with other molecules, it is crucial to know its composition, shape, and precise dimensions. With all this information, we can now:

- ✓ **Design medicines**. Most drugs work by interacting with specific proteins in the body, and knowing the structure of these proteins allows scientists to design drugs that precisely fit their active sites, optimizing their effectiveness and reducing side effects. For example, in the development of antivirals or cancer treatments, molecules are designed to block essential functions of the proteins in viruses or malignant cells.

- ✓ **Perform what is known as protein engineering**: Understanding how a protein folds in three dimensions opens up the possibility of modifying it or designing new proteins with specific functions, such as enzymes that degrade plastic pollutants or proteins that act as innovative vaccines. These advances are crucial in biotechnology and biomedicine.

- ✓ **Understand diseases**: Many diseases, such as Alzheimer's or Parkinson's, are related to protein misfolding. Knowing the normal and pathological structures allows for the development of targeted therapies that can prevent or reverse these changes. Additionally, understanding the structure of proteins involved in autoimmune or infectious diseases is vital for developing specific treatments.

- ✓ **Innovate in biotechnology and sustainability**: By designing proteins that do not exist in nature, it is possible to create solutions for environmental problems, such as enzymes that can break down plastics or generate biofuels efficiently. These developments have a direct impact on sustainability and the creation of new biotech industries.

In summary, protein structure is a crucial map that guides scientists in creating therapies, understanding diseases, and developing biotechnological innovations that can transform both medicine and industry.

The Laureates' Developments Did Not Start from Scratch

Aside from the laureates' merits and the undeniable importance of their contributions, it is important to recognize that these advances were made possible thanks to the prior development of entirely experimental scientific procedures and the accumulation of information generated over decades by these tools, such as Nuclear Magnetic Resonance (NMR) and, very specifically, by Crystallography — that is, the use of X-ray interaction with crystals, which has been yielding results since the early 20th century when applied to simple compounds. However, it was from the early 1970s that Crystallography began to be applied to crystals obtained from biological macromolecule solutions. Crystallography has led to 29 Nobel Laureates

since the early 20th century and, to date, to the experimental knowledge of the structure of more than 225,000 biological macromolecules. Therefore, it is thanks to this vast amount of pre-existing experimental information, along with the advancement of artificial intelligence (AI), that Demis Hassabis and John Jumper have been awarded the 2024 Nobel Prize in Chemistry for developing the tool called AlphaFold 2, based on AI. This significant development is already giving a remarkable boost to Crystallography applied to structural biology, as the models provided by AlphaFold 2 are, in most cases, excellent starting points for the experimental resolution of proteins' three-dimensional structures. Once the theoretical protein folds proposed by AlphaFold 2 are known, Crystallography can expand this molecular information with very high precision, determining their interactions with drugs or the structures of their macromolecular complexes—all with enough rigor to understand even the smallest details of the biological world, as it is often these minute details that lead to a complete understanding of the structural secrets of these life-sustaining machines.

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October 12, 2024