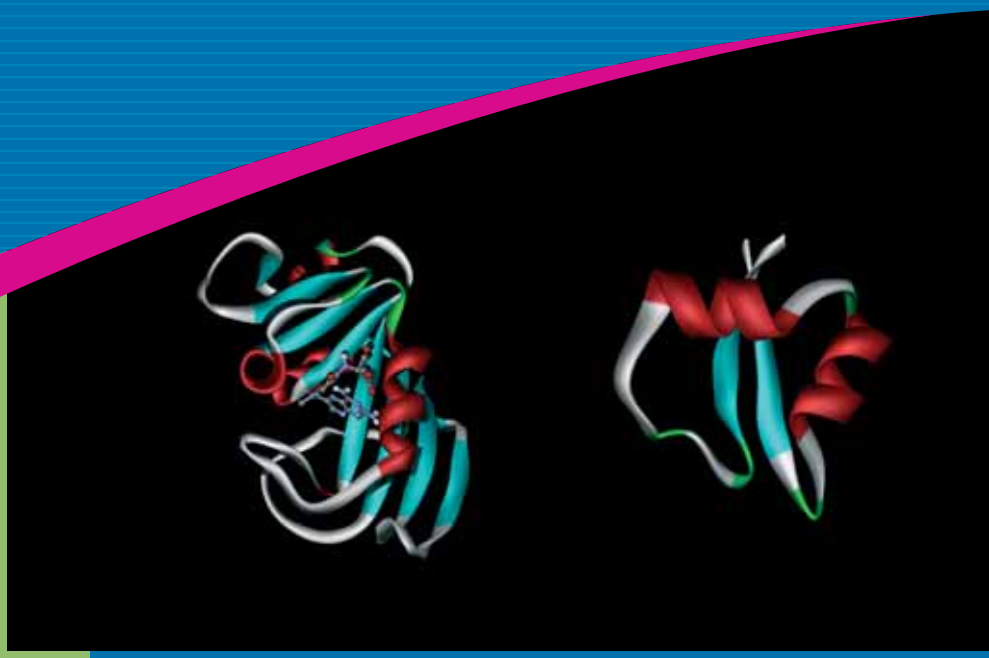

The project will focus on protein folding.

Emerging complexity in protein folding

Complexity has a key role to play in biology yet is still poorly understood. A European project, EMBIO, aims to provide the research community with new methodologies based on innovative mathematics and software to help make sense of the dynamics of self-organisation. By focusing on the emergence of complexity in protein folding, the project team will be addressing one of the major problems in modern biology, and their results will have important implications for drug discovery.

Complexity and self-organisation are critical to many biological systems, yet many questions about how complexity emerges from simpler starting states remain unanswered. Current computer simulations of complex systems in biology take many hours to achieve a rather poor copy of what Nature manages perfectly in a split second. The EMBIO project, part of the NEST-PATHFINDER initiative on 'Tackling complexity in science', aims to provide new tools and approaches to help answer some of these questions. By focusing on one of the major challenges in modern biology – protein folding – they hope to identify the fundamental principles governing the emergence of complexity in self-organising biomolecular systems.

The interdisciplinary research consortium, comprising eight European laboratories with expertise in mathematics, statistical physics, chemistry, information theory, biology and computing, will develop highly innovative mathematical and computational approaches to characterise the dynamics of self-organisation and apply these to protein structure.

Because of its focus on protein folding, EMBIO will have a particular impact in molecular and structural biology, but its innovative approach to analysing complexity will be relevant to many other systems that give rise to self-organisation.

From chaos to calm

Protein folding is a striking example of emergent complex behaviour and, being well defined, it is an ideal system in which to study complexity. Most proteins spontaneously and reproducibly fold from an arbitrary chain of amino acids to a specific 3D structure adapted to their biological function. But although data exists on the chemical compositions and structures of thousands of proteins, it is still not possible to predict accurately or to explain how and why this transition to a folded structure takes place, partly because it is a non-linear, dynamic process influenced by many factors.

As the protein's final 3D structure is considered the most thermodynamically stable one, scientists currently use a 'folding funnel' model to explain the dynamics of the transition. Initially, the chaotic motions of the atoms have high levels of free energy and occupy large areas of potential folding space. As the protein molecule folds and its free energy decreases, the available space is reduced to the point where the molecule

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EMBIO

Improved understanding of protein folding is vital to the pharmaceutical industry.

AT A GLANCE

Official title
Emergent organisation in complex biomolecular systems

Coordinator
UK: University of Cambridge

Partners
- *Austria: University of Vienna*
- *Germany: Friedrich-Schiller-University Jena*
- *Germany: University of Heidelberg*
- *Germany: University of Leipzig*
- *Italy: University of Florence*
- *Sweden: Chalmers University of Technology*
- *The Netherlands: University of Groningen*

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Web: http://www.cordis.lu/nest

is 'forced' into its final structure, corresponding to its minimum energy.
Whilst this model is now generally accepted, it does not explain many aspects of protein folding, notably the speed at which it takes place. The EMBIO consortium will develop a new computational approach which will provide a more accurate description of the dynamics involved, taking into account temporal, topological, statistical and dynamic properties. Powerful state-of-the-art computing facilities available within the consortium will enable sophisticated 'all atom' simulations of folding and the generation of new data on which to base novel methods and algorithms.

Advances in understanding protein folding will bring much needed innovation to the drug discovery business.

An alternative view

The new methodologies developed by EMBIO, underpinned by innovative mathematical approaches and applications software, will open the door to an alternative view on protein folding. A greater understanding of how proteins fold is likely to bring strategic benefits and much needed innovation to drug discovery. Most new drugs target specific proteins in the body. In addition, misfolded proteins are directly implicated in a number of debilitating conditions such as Alzheimer's and Creutzfeldt-Jakob disease.

The consortium also expects its work on complexity estimation to impact on areas of study involving complicated chaotic dynamics. Examples of these are heart rhythms, where a better understanding of their chaotic nature could lead to new diagnostic tools for heart disease, and electromagnetic signals, which are generated in photonic devices used for optical communication.
More generally, if EMBIO succeeds in identifying the generic features which characterise dynamic complexity, their results will be widely applicable by the scientific community for the study of complexity in areas as diverse as social science or forest fires.

SIXTH FRAMEWORK PROGRAMME