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Editorial

Structural biology stands at a crossroads built of success. A decade ago, three-dimensional structures of single, relatively small proteins and nucleic acid fragments were considered triumphs in themselves. Now, structure determination is becoming more routine for many of these macromolecules, and structural analysis of larger or more complex biological systems is increasingly feasible. This trend is exemplified by the recent atomic descriptions of ion channels, rhodopsin, RNA polymerase II, the ribosome, and the multimodular fatty acid synthases. While much work remains to be done, the underlying structural foundation of many core processes in biology has been determined, or is nearing completion.

Despite this progress, many challenges remain ahead for structural biology. Structures are still rare or nonexistent for many multicomponent systems and membrane proteins such as G-protein coupled receptors. Moreover, large biomolecular assemblies are often transient and heterogeneous, complicating their structural characterization by traditional methods. Even when structures are resolved, the link between structure and mechanism is often tenuous, and details about the coupling of macromolecular dynamics, thermodynamics, and mechanism are needed to validate and enhance structural models. In addition, it remains difficult to elucidate how structures have evolved, how to control and modify their properties, and how to design new systems. For a journal called *Structure*, it is a time to showcase compelling work in all of these fields.

Structure originally focused on describing the structures of biological molecules, the rules of their folding, and the principles of biomolecular design. The journal has evolved over the last several years to place a higher premium on biological function, particularly on structure/function relationships in systems that illuminate biology in eukaryotic organisms. X-ray crystallography and NMR spectroscopy approaches provide exceptional insights into biological function, and *Structure* continues to encourage submission of manuscripts detailing macromolecular structures and their interactions at atomic resolution. We favor structural studies that include biochemical and biophysical analyses, since such studies vastly augment the impact of structural work, as well as those reports on structures that deal with two or more macromolecular components, as these structures often provide vital insights into macromolecular interactions. Manuscripts restricted to structure determination of a single entity will usually only merit publication in *Structure* if the molecule is of unusually high interest or the structure presents a substantial conceptual advance.

The complexity of systems undergoing structural analysis is increasing. We are excited about the prospect that structural biology will continue to contribute to our understanding of larger and more intricate biological assemblies, despite the fact that these studies often involve resolution of static structures at low to moderate resolution. Correspondingly, *Structure* encourages submission of studies using low-resolution crystallography, cryoelectron microscopy, and other imaging techniques.

We continue to support theoretical and computational approaches that are grounded in structure, especially if they are directed at explaining mechanism or evolution, include new experimental results, or are based on significant methodological advances.

Dynamic behavior in biological processes underlies mechanism. NMR spectroscopy, single-molecule fluorescence, kinetic analysis, and other forms of spectroscopy are particularly well-suited to address directly the link between structure, dynamics, and mechanism. Therefore, *Structure* encourages submission of studies that utilize these approaches to monitor biological dynamics.

Fundamental issues still exist with respect to how biological macromolecules achieve their native, folded state. Reports detailing experimental or computational studies that address folding, misfolding, and their role in biological function and disease remain an interest of the journal.

Finally, the abundant success of structural biology has been driven by extraordinary technological advances in x-ray crystallography, NMR spectroscopy, and electron microscopy. This trend will only grow, and *Structure* promotes publishing significant methodological advances in these and other emerging structural biology techniques, chiefly through our Technical Advances and Ways & Means formats.

From x-ray crystallography, NMR spectroscopy, and electron microscopy to protein folding and conformational dynamics, and from significant new biological insights to technical advances and computational approaches, *Structure* aims to present structural and molecular biologists with a full spectrum of exciting and innovative research. As both Editors and active scientists working in the field, together with the Associate Editor located in the Cell Press offices, we are committed to providing a home for structural biology research where authors receive constructive reviews from their peers in a timely way with rapid publication of accepted papers.

The future of *Structure* and structure are intimately linked. As methods for structural determination have become more developed, and, in some cases, automated, the barrier for entry into the world of structure has been lowered, thus enabling scientists who would not describe themselves as structural biologists to incorporate structure determination as a tool in their investigative toolbox. These advances have also allowed many structural biologists to investigate more complex biological systems with an expanded repertoire of experiments. The broad definition of structural biology outlined here, rooted in more traditional structural studies and embracing a wide range of approaches that includes molecular biology, single-molecule spectroscopy, force measurements, and computational approaches, underscores our central conviction that a combination of techniques aimed at elucidating the atomic and molecular underpinnings of macromolecular function will afford the greatest opportunities for understanding biological systems.

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