Matthew Baker, PhD
Assistant Professor
Biochemistry and Molecular Biology

De Novo Modeling Building in CryoEM Density Maps

Matthew Baker, PhD, recently joined The University of Texas Health Science Center at Houston as an Assistant Professor in the Department of Biochemistry and Molecular Biology. Dr. Baker's laboratory focuses on the development and application of computational modeling tools for the analysis of macromolecular assemblies. With over 20 years of experience in electron cryomicroscopy (cryoEM) and computational modeling, his pioneering efforts produced the first C-alpha backbone and all-atom models directly from near-atomic resolution cryoEM density maps without the aid of a structural template. Today, Dr. Baker's class-leading computational tools are used to analyze and model a wide range of challenging structures, including cancer immunotherapeutic, viruses and membrane proteins. In addition to his research, Dr. Baker is the faculty liaison and mentor for BRASS, a scholarship program for incoming graduate students at BCM, and the director of Brain Labs, a STEM outreach program in neuroanatomy.

Abstract: Over the course of the last two decades, single particle electron cryomicroscopy (cryoEM) has emerged from "blob-ology" and can now routinely produce structures at resolutions that readily allow for atomistic interpretations directly from a density map without the aid of structural templates. This rapid improvement in obtainable resolutions is in part due to the technological advancements in electron microscopes, imaging hardware and tools for data processing. Concurrently, new model building tools have been developed, enabling atomistic model generation in complex density maps at resolutions better than 5Å. Our computational modeling software, Pathwalking, is a robust suite of tools that can rapidly and reliably generate accurate models directly from near-atomic resolution density maps without any structural template or a priori knowledge. In fact, the core algorithm in Pathwalking is agnostic to the protein sequence, building a model based purely on the optimization of protein geometry in the density map. As Pathwalking is extremely quick (on the order of a few seconds for even the largest proteins), the software can generate a gallery of potential models, as well as a probabilistic model, in minutes. These tools have been used on a number of challenging cryoEM density maps, including membrane proteins and viruses, to enable the discovery of macromolecular structure and function.