Predicting protein DYNamics using Normal Modes and Deep Learning

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Protein structure prediction has significantly advanced in recent years, to the point where the single-sequence, single-structure approximation has broken down. While AlphaFold2 and its counterparts enable breakthroughs today, the challenge of tomorrow is already clear: modeling protein dynamics. The objective of dyNMDL is to develop a novel physicsbased approach to describe the functional dynamics of proteins, based on normal mode analysis and validated with NMR data, along with a deep-learning model based on transformers, which will be trained by leveraging transfer learning from relevant published models. Our approach, supported by the observation of the existence of evolutionary pressure on protein functional dynamics, relies on a large-scale analysis of the evolutionary conservation of protein dynamics and is among the first to enable end-toend prediction of dynamics from the sequence, with significant implications in structural biology, drug discovery, and protein design.

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