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Memory Protein

When UC Santa Barbara materials scientist Omar Saleh and graduate student Ian Morgan sought to understand the mechanical behaviors of disordered proteins in the lab, they expected that after being stretched, one particular model protein would snap back instantaneously, like a rubber band.

Instead, this disordered protein relaxed slowly, taking tens of minutes to relax into its original shape — a behavior that defied expectations, and hinted at an inner structure that was long thought to exist, but has been difficult to prove.

“The speed of relaxation is important because it gives us some insight into the structural organization of the protein,” said Morgan, the lead author in a paper published in Physical Review Letters. “This is important because the structural organization of a protein is usually related to its biological function.”

While a protein with fixed ‘folds’ — a well-defined three-dimensional structure — is associated with its function, disordered proteins, with their unstable structures, derive their functions from their dynamics.

“More than 40% of human proteins are at least partially unfolded, and they are often linked to critical biological processes as well as debilitating diseases,” Morgan said.

The slow relaxation is in fact a behavior typically reserved for folded proteins.

“In the 1980s it was discovered that folded proteins exhibit slow relaxations,” Morgan said, in a behavior typical of glasses — a class of materials that are neither

truly liquid nor crystalline solid states, but can exhibit characteristics of either state.

“We have been studying folded proteins for a long time and have developed a lot of good tools for them, so it was quickly figured out that the slow relaxations could be explained by a mechanism by which ‘frustrated’ molecules trying to fit themselves in a small space,” Morgan said — a mechanism called “jamming.” “This explanation helped us better understand the structure of folded proteins and explain glassy behavior in a lot of other systems.”

However, the protein, which the researchers were trying to stretch by means of a device known as a magnetic tweezer, was a disordered protein. By definition, it wasn’t trying to pack many molecules into a small space, so it shouldn’t run into the jamming problem, Saleh said.

“So, when we observed slow relaxations, it either meant our definition of the protein was wrong or there had to be another mechanism,” Morgan said.

Furthermore, by allowing the stretched protein to relax but stretching it again with less force before it had a chance to fully relax, the researchers found that the protein “remembered” its previous stretching — initially lengthening, as expected with more force, but eventually slowly relaxing again lengthening as expected with less force, but then slowly relaxing over time. Conceptually, Morgan explained, the longer the protein is stretched the longer it takes to relax, hence it “remembers” how long it was pulled.

To explain these unexpected, glassy behaviors, the researchers drew inspiration from some rather mundane objects: crumpled paper and memory foam. Both structurally disordered systems, they exhibit a similar slow, logarithmic relaxation after being subjected to forces, and particularly in the case of the foam, a “memory” effect.

For the researchers the behaviors suggested that like memory foam and crumpled paper, the internal structure of the protein was not one of a single, fixed unit, but one of several, independent substructures of a range of strengths between strong and weak that respond to a range of forces exerted on the material along different lengths of time. For instance, strong structures may withstand a certain amount of strain before being pulled apart and be the first to relax, whereas weak structures will stretch with smaller forces and take longer to relax.

Based on this notion of multiple substructures and confirmed with experimental data, the researchers determined that the protein’s logarithmic relaxation rate is inversely proportional to the stretching force.

“The stronger the stretching force applied to the disordered protein, the more the protein relaxed in the same amount of time,” Saleh explained.

“Mechanical disordered systems with similar structural arrangements tend to be remarkably durable,” Morgan said. “They also have different mechanical properties depending on how much you pull and compress them. This makes them very adaptable, depending on the magnitude and frequency of the force.” Understanding the structure behind this ability to adapt could open the door to future dynamic materials, that, Morgan said, “just like your brain, helps them filter out unimportant information and makes them more efficient at storing repeated stimuli.”

Research on this study was conducted also by Ram Avinery, Gil Rahamim and Roy Beck at Tel Aviv University.

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