EXECUTIVE SUMMARY [NON-TECHNICAL ABSTRACT FOR PUBLIC INFORMATION OR PROGRAM PROMOTION]:
State **in layman's terms** the application's broad, long-term objectives and specific aims, making reference to the potential public benefits of the project relevant to California.

Neurotrophins (NTs) are proteins that act as switches to initiate the transmission of various types of signals, including processes in the brain that affect learning and memory. There is widespread interest in designing drugs that will supplement NT activity to treat a wide range of conditions including chronic pain, stroke and Alzheimer's disease. The quality of the drug, however, will depend on whether it can hit a particular target, thereby preventing the side effects that would occur if the drug were less specific. Currently, scientists are not sure what causes one type of NT protein to bind to a target (its receptor), while other types cannot. It is also not understood how this interaction triggers signal transmission. We hypothesize that the specificity of the NT/receptor interaction as well as the resulting transmitted signal are influenced by the shape and degree of flexibility in both molecules. We will begin by studying the interaction between the neurotrophin BDNF with its receptor, looking with atomic resolution to see how the flexibility changes when the proteins interact versus when they are alone, and also whether the impact of the interaction is felt in regions of each protein that are far away from the site of contact. Eventually our research will look at these motions in many NTs, and allow us to compare the differences. In the long term, our research will provide insight into how signals are transmitted as a result of the interactions, thereby helping scientists design drugs to treat various neurological problems.