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### **Principles of allosteric mechanisms in cell signaling**

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Linking cell signaling events to the fundamental physicochemical basis of the conformational behavior of single molecules and ultimately to cellular function are key challenges facing the life sciences. Specific protein function is determined by the extent to which the protein populates a distinct active state. Allostery, an inherent physical property of proteins, is a key factor governing the relative populations among accessible conformational states. Allostery can be defined as the change in the distribution of the conformational ensemble through some perturbation. Nature has co-evolved ligand-host protein interactions, optimizing them to tune the populations of the active (or inactive) states for function, either by stabilizing the active conformation and/or destabilizing the inactive conformations, or vice versa. More and more data attest to the significance of allostery in cell life under physiological conditions and in disease. We aim to delineate key challenging questions, such as can we predict a priori- and quantify- changes incurred by allosteric mutations or specific binding events to increase/decrease the population of the active or inactive state to up- or down- regulate the protein? I will provide an overview of the fundamental underpinnings of allostery.