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Enzymes and liquid-liquid phase separation: regulation of the enzymatic activity and modulation of the biomolecular condensate material properties

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Enzymes play fundamental roles in almost all life processes. They are biological catalysts able to substantially increase the rate constants of a great variety of chemical reactions, thus controlling energy transduction and signaling, as well as the transcription and translation of genetic information. Therefore, they have an important role in regulating the metabolism of cells and there is a broad interest in understanding the origin and the mechanism of this catalytic power on a molecular level. Importantly, during catalysis they release energy, creating transient mechanical stresses and chemical gradients. The compartmentalization of enzymes within membrane-enclosed organelles has represented the natural framework for the spatiotemporal regulation of metabolic reactions in the cell. However, the recent discovery of membrane-less liquid-like compartments, called biomolecular condensates (BMCs) has forced the scientific communities to look at the metabolism regulation under a new perspective. BMCs often form through a process called liquid-liquid phase separation (LLPS). LLPS allows the formation of at least two different phases, one dense phase formed by concentrated biomolecules (proteins and/or nucleic acids) that usually interact by multivalent interactions and the surrounding diluted phase, depleted of biomolecules. The process of BMC formation is dynamic and reversible. The potential of BMCs to selectively sequester enzymes (and other molecules) from the cellular environment in a more flexible and dynamic manner has introduced a novel regulatory mechanism in biology and biochemistry, whose full potential is under investigation from several points of view. Here, we present how the enzymatic activity can be regulated within biomolecular condensates and the effects of the enzymatic activity on the material properties of the biomolecular condensates.