Abstract: The three-dimensional genome organization plays an essential role in all DNA-templated processes, including gene transcription, gene regulation, DNA replication, etc. Coarse-grained models parameterized to reproduce experimental data via the maximum entropy optimization algorithm serve as effective means to study genome organization at various length scales. They have provided insight into the principles of whole-genome organization and enabled de novo predictions of chromosome structures from epigenetic modifications. In addition, they provided insight into the critical role of the chromatin network in stabilizing multiple liquid droplets. Applications of these models at a near-atomic resolution further revealed physicochemical interactions that drive the phase separation of disordered proteins and dictate chromatin stability in situ.