Mapping atomic models back into cells - visual proteomics and in situ structure determination.

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A new spin, on an old computer vision technique, template matching, enables us to use the high-resolution details provided by macromolecular models determined by MX, NMR or cryoEM to determine the location and orientation of macromolecules in images of frozen-hydrated cells. Compared to classic detection approaches, like 3D template matching in tomograms, the extra information used in our approach enhances the specificity of detection, raising the level of "surprise" one would have to measure a false-positive detection. Aside from providing a means to determine where (and when) a particular complex may be in a cell, the approach also enables us to "fish" out interacting partners. For example, we can search a cell with a limited subset of stable 50S ribosome proteins and RNAs, and reconstruct volumes that contain information not found in the template, like conformationally variable 30S components as well as other translational cofactors. Detection in situ is currently limited to targets that have a molecular mass of ~300-400 kDa. I will present work in our lab to reduce that mass limit by improving our radiation damage model as well as incorporating a more complete description of inelastic scattering in our forward model used to generate templates for the approach.