Building site for molecular complexes

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Often the sum is greater than its parts. Using an atomic force microscope as a “crane”, Ludwig Maximilian University of Munich researchers have succeeded in bringing two biomolecules together to form an active complex – with nanometer precision and built-in quality control.

The business end of the atomic force microscope (AFM) is its needle-sharp tip. It can be used to pick single molecules from a substrate and move them to specific positions with the precision of a few nanometers. This “single-molecule cut-and-paste” procedure was developed by LMU physicist Professor Hermann Gaub, and he and his colleagues have now used it to assemble a functional molecular complex from inactive, single-molecule building blocks.

They built the complex from two short strands of RNA, picking one from a depot with the AFM, and placing it close to the second strand deposited elsewhere on the substrate. When the two RNA segments come into contact, they spontaneously form what is called an “aptamer”, a three-dimensional binding pocket for a target molecule – in this case the fluorescent dye malachite green. The binding interaction amplifies the fluorescence emitted by the target more than 1000-fold - and signals that the two parts of the aptamer have assembled correctly.

“The important thing is that we have precise mechanical control over the assembly process,” says lead author Mathias Strackharn. “When we see the malachite-green signal in the fluorescence microscope, we know that the aptamer has been successfully reconstituted.” The researchers are now in a position to construct other systems whose natural function

depends on the configuration of their molecular components. This will enable them to dissect how interactions between their parts mediate the functions of molecular complexes.

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