CLAIMS

1. A method comprising:

    a) providing:

        i) two plasmonic particles;

        ii) a nucleic acid scaffold coupled to the two plasmonic particles; and

        iii) a protein, wherein the protein is bound to the nucleic acid scaffold; and

    b) with aid of the two plasmonic particles, generating an electrical field at the protein bound to the nucleic acid scaffold.

2. The method of claim 1, wherein (a) further comprises contacting the protein with a nucleic acid analyte and a labelled nucleotide.

3. The method of claim 2, further comprising determining a sequence of the nucleic acid analyte.

4. The method of claim 2 or 3, further comprising detecting the labelled nucleotide.

5. The method of any one of claims 2-4, wherein the labelled nucleotide comprises a fluorophore.

6. The method of claim 5, further comprising modulating a fluorescence emission of the fluorophore with the electric field.

7. The method of any one of claims 1-6, wherein (a) further comprises providing a nucleic acid analyte bound to the nucleic acid scaffold.

8. The method of any one of claims 1-7, further comprising detecting an order of fluorescence emissions from labelled nucleotides that are incorporated by the protein.

9. The method of claim 8, wherein the labelled nucleotides comprise one or more species; wherein each species of the labelled nucleotides comprises a distinct fluorescence emission signature; and wherein the distinct fluorescence emission signature is distinguishable by differences in peak emission wavelength, differences in fluorescence emission intensity, differences in fluorescence emission duration, differences in duration between successive fluorescence emissions, or any combinations thereof.

10. The method of any one of claims 1-9, wherein the two plasmonic particles are bound to the nucleic acid scaffold and positioned relative to one another such that a plasmonic hotspot exists between the two plasmonic particles; wherein the plasmonic hotspot comprises a region unoccupied by the nucleic acid scaffold, wherein the region unoccupied by the nucleic acid scaffold is defined by a three-dimensional space having a length (L) between the two plasmonic nanoparticles, a height (H) at a midpoint (L/2) that is perpendicular to (L), and a width (W) at L/2 that is perpendicular to L and H, wherein W is selected from 20 nanometers (nm) to about 100 nm, wherein H is selected from 10 nm to about 100 nm, and wherein L is measured at the shortest distance between the two plasmonic nanoparticles.

11. The method of claim 10, wherein the region unoccupied by the nucleic acid scaffold has a volume of at least about 1 zeptoliter (zL).

12. The method of claim 10 or 11, wherein the region unoccupied by the nucleic acid scaffold is 80% or more of the plasmonic hotspot.

13. The method of any one of claims 1-12, wherein each of the two plasmonic particles are coated with a coating, and wherein the coating reduces aggregation of the two plasmonic particles by 50% or more relative to the two plasmonic particles lacking the coating.

14. The method of any one of claims 1-13, wherein the nucleic acid scaffold comprises DNA origami structures, and wherein at least a portion of the DNA origami structures are assembled to form a U-shaped or curved structure.

15. The method of any one of claims 1-14, wherein the protein is a nucleic acid polymerase.