CLAIMS

WHAT IS CLAIMED IS:

1. A method for single molecule sensing comprising:

forming a ternary complex by contacting a molecular sensor with at least one charge modulator, wherein the ternary complex is bound to a charge sensor, and contacting the molecular sensor with the at least one charge modulator generates a change in current;

measuring the change in current;

correlating the change in current with a presence of the at least one charge modulator, thereby sensing a single molecule; and

removing the ternary complex from the charge sensor.

2. The method of claim 1, wherein the single molecule comprises a nucleic acid.

3. The method of claim 1, wherein the charge sensor comprises a graphene-enabled field effect transistor (GeFET) or CMOS device.

4. The method of claim 1, wherein the molecular sensor is in electrical communication with the charge sensor.

5. The method of claim 1, wherein the molecular sensor comprises a polymerase.

6. The method of claim 1, wherein the at least one charge modulator comprises a charge

modulating nucleotide (CMN), and wherein the CMN comprises at least one modification relative to a canonical nucleotide.

7. The method of claim 1, wherein the ternary complex further comprises a polynucleotide primer, and the method further comprises incorporating a CMN into the polynucleotide primer.

8. The method of claim 1, wherein the change in current is 1 nanoamp to 100 picoamps.

9. The method of claim 1, wherein the change in current is at least 1.01-3 times a background current.

10. The method of claim 1, wherein 1-200 single molecules are sensed per second.

11. A method for single molecule polynucleotide sequencing comprising:

contacting a plurality of polynucleotides with at least one primer and at least one polymerase to form a plurality of ternary complexes, wherein the plurality of ternary complexes comprise a graphene binder;

detecting one or more bases of the polynucleotides in real time, wherein detection occurs when the plurality of ternary complexes are bound to a graphene layer of a device, wherein the device is a chemically sensitive field effect transistor device or a CMOS device; and

removing the ternary complexes from the graphene layer of the device.

12. The method of claim 11, wherein the graphene binder comprises an aromatic group.

13. The method of claim 11, wherein detecting comprises measuring a change in current when a charge modulating nucleotide (CMN) is incorporated into the at least one primer.

14. The method of claim 13, wherein the change in current is:

1 nanoamp to 100 picoamps; and/or

1.01 to 3 times a background current.

15. The method of claim 12, wherein the graphene layer has a thickness of 1 to 5 atoms.

16. The method of claim 11, wherein the chemically sensitive field effect transistor device comprises:

a solid support, wherein the solid support comprises a plurality of loci, wherein each loci comprises:

a graphene layer;

a gate electrode;

a drain electrode, wherein the gate electrode and the drain electrode are in electrical communication via the graphene layer; and

at least one insulating layer, wherein the at least one insulating layer is located between the gate electrode and the drain electrode.

17. The method of claim 16, wherein the chemically sensitive field effect transistor device further comprises at least one ground shield, and wherein the at least one ground shield

comprises an opening which permits electrical communication between the graphene layer and at least one buried gate.

18. The method of claim 16, wherein the gate electrode and drain electrode are configured such that an amount of current that passes from the gate electrode to the drain electrode is dependent on a property of the ternary complex.

19. The method of claim 1, wherein removing the ternary complex comprises washing with a solvent, and wherein the solvent comprises acetonitrile, methanol, ethanol, 2-propanol, acetone, dimethylformamide, formamide, tetrahydrofuran, or dimethyl sulfoxide.

20. The method of claim 1, wherein the molecular sensor is conformationally labeled, wherein the conformational label is responsive to: a change in a structure of the molecule, a change in a shape of the molecule, or a change in an arrangement of parts of the molecule.