CLAIMS

1. A sequence-detection system that detects a sequence of entities within a target, the sequence-detection system comprising:

a mechanical-change sensor that sequentially interacts with each of multiple entities within the target and that exhibits one or more mechanical changes, mechanical changes including changes in shape, position, and orientation of the mechanical-change sensor, when the mechanical-change sensor specifically interacts with each entity, each entity having a type corresponding to one or more physical characteristics that differentiate the entity from entities of other types, wherein physical characteristics include shape, composition, and structure;

a mechanical-change-to-signal transducer that transduces the one or more mechanical changes into a time-varying electrical voltage signal;

an analysis subsystem that determines a sequence of entity types within the target using the time-varying electrical voltage signal; and

a control subsystem that

initializes the sequence-detection system in accordance with one or more operational parameters of the sequence-detection system, and

controls the sequence-detection system to generate, collect samples of, and analyze the time-varying electrical voltage signal to determine the sequence of entity types within the target.

2. The sequence-detection system of claim 1

wherein the target is a primer-associated nucleic-acid template polymer;

wherein the entities are nucleotide monomers;

wherein the mechanical-change sensor is a nucleic-acid-polymerase mechanical-change sensor contained within a first solution-containing chamber; and

wherein the mechanical-change-to-signal transducer further comprises

a variable resistor that regulates flow of an electrical current through a porin channel that provides fluid communication between the first solution-containing chamber and a second solution-containing chamber,

a mechanical coupler that couples the mechanical-change component to the variable resistor, and

a current-to-voltage converter that outputs a time-varying electrical voltage signal that varies in correspondence with the rate of flow of the electrical current through the porin channel.

3. The sequence-detection system of claim 2 wherein the operational parameters include:

a voltage magnitude of a read voltage applied across the porin channel and a polarity of the read voltage;

a voltage magnitude of a noise-inhibition voltage applied across the porin channel and a polarity of the noise-inhibition voltage;

a voltage magnitude of a configuration voltage applied across the porin channel and a polarity of the configuration voltage.

4. The sequence-detection system of claim 3

wherein the polarity of the noise-inhibition voltage is opposite from the polarity of the read voltage; and

wherein the polarity of the noise-inhibition voltage is opposite from the polarity of the configuration voltage.

5. The sequence-detection system of claim 3 wherein the control subsystem configures the sequence-detection system by:

applying the configuration voltage across the porin channel with the configuration-voltage polarity to seat the nucleic-acid-polymerase mechanical-change sensor within the porin.

6. The sequence-detection system of claim 5 wherein, following configuration of the sequence-detection system, the control subsystem adjusts the read-voltage magnitude to position a reporter region of a nucleic-acid -polymer tether at a reference displacement.

7. The sequence-detection system of claim 3 wherein, following configuration of the sequence-detection system, the control subsystem controls the sequence-detection system to

generate, collect samples of, and analyze the time-varying electrical voltage signal to determine the sequence of entity types within the target by:

iteratively

applying the read voltage across the porin channel with the polarity of the read voltage for a first time period, during which the time-varying electrical voltage signal is sampled, stored in a memory, and analyzed by the analysis subsystem, and

applying the noise-inhibition voltage across the porin channel with the polarity of the noise-inhibition voltage for a second time period

until a termination condition occurs.

8. The sequence-detection system of claim 7 wherein the lengths of the first and second time periods are specified by operational parameters.

9. The sequence-detection system of claim 7 wherein termination conditions include:

a power-off event; and

a decrease in a rate of sequence-information generation below a threshold level by the sequence-detection system.

10. The sequence-detection system of claim 2 wherein the operational parameters include:

temperature;

pH of the solutions in the first and second solution-containing chambers; and

the contents of the solutions in the first and second solution-containing chambers.

11. The sequence-detection system of claim 10 wherein the operational parameter related to the contents of the solutions in the first and second solution-containing chambers encompasses one or more of:

one or more types of ionized salts in the solutions;

concentrations of the one or more types of ionized salts in the solutions;

one or more types of nucleotide polyphosphates in the solution in the first solution-containing chamber;

concentrations of the one or more types of nucleotide polyphosphates in the solution in the first solution-containing chamber;

one or more types of primer-associated nucleic-acid template polymers in the solution in the first solution-containing chamber;

concentrations of the one or more types of primer-associated nucleic-acid template polymers in the solution in the first solution-containing chamber; and

a type and structure of a nucleic-acid-polymer tether.

12. The sequence-detection system of claim 10 wherein the operational parameter related to the contents of the solution in the in the solution in the first solution-containing chamber is adjusted to control the rate of sequential specific interaction of the mechanical-change sensor with entities within the target.

13. The sequence-detection system of claim 10 wherein a primer with a 3' dideoxynucleotide monomer is employed to constrain the sequence-detection system to specifically interact with a single entity.

14. The sequence-detection system of claim 2 wherein a signal response of the sequence-detection system is configured by selecting a reporter region with a nucleotide-monomer sequence corresponding to the signal response.

15. A method that determines a sequence of entities within a target, the method comprising:

initializing a sequence-detection system in accordance with one or more operational parameters of the sequence-detection system, the sequence-detection system having

a mechanical-change sensor that sequentially interacts with each of multiple entities within the target and that exhibits one or more mechanical changes, mechanical changes including changes in shape, position, and orientation of the mechanical-change sensor, when the mechanical-change sensor specifically interacts with each entity, each entity having a type corresponding to one or more physical characteristics that differentiate the entity from entities of other types, wherein physical characteristics include shape, composition, and structure,

a mechanical-change-to-signal transducer that transduces the one or more mechanical changes into a time-varying electrical voltage signal, and

an analysis subsystem that determines the types of entities within the target using the time-varying electrical voltage signal; and

controlling the sequence-detection system to generate, collect samples of, and analyze the time-varying electrical voltage signal to determine the sequence of entity types within the target.

16. The method of claim 15 further including controlling the sequence-detection system to produce a particular signal response to the entities within the target by selecting a reporter region with a nucleotide-monomer sequence corresponding to the signal response.

17. The method of claim 15 further including controlling the sequence-detection system to determine the type of an entity at a particular position within the target by modifying the target to permit the mechanical-change sensor to specifically interact only with the entity at the particular position.

18. The method of claim 15 further including controlling the sequence-detection system to configure the sequence-detection system by:

applying a force to mount the mechanical-change sensor to the mechanical-change-to-signal transducer; and

detecting a signal characteristic of the sequence-detection system when the mechanical-change sensor is mounted to the mechanical-change-to-signal transducer.

19. The method of claim 15 wherein the initializing the sequence-detection system in accordance with one or more operational parameters further includes initializing the sequence-detection system in accordance with one or more operational parameter values selected to control the mechanical-change sensor to sequentially specifically interact with entities within the target with a specific average time of specific interaction.

20. The method of claim 15 further including controlling the sequence-detection system to calibrate the sequence-detection system by applying a force to select relative positions for two subcomponents of the mechanical-change-to-signal transducer.