

WHAT IS CLAIMED IS:

- 1 1. 1. A system for high-throughput nucleic acid sequencing comprising:
2 a reaction subsystem for carrying out biochemical sequencing reactions on
3 nucleic acid samples in reaction units;
4 a discrete detection subsystem for capturing optical images of the sequencing
5 reactions to be used for analysis of the optical images independently of the sequencing
6 reactions; and
7 a coupling subsystem for transferring the nucleic acid samples between the
8 reaction platform and the detection system whereby the reaction platform and the detection
9 systems are physically loosely coupled in a reversibly integrated system.
- 1 2. The system according to claim 1, wherein the reaction subsystem
2 comprises:
3 at least one discrete reaction platform configured to permit interchangeable
4 utilization of a plurality of discrete reaction platforms.
- 1 3. The system according to claim 2, wherein the reaction platforms
2 comprise:
3 a plurality of reaction units, each reaction unit containing at least one
4 individual flow cell that is removable from the reaction platform.
- 1 4. The system according to claim 3, wherein said coupling subsystem
2 comprises:
3 a carrying device having a gripping mechanism operative to select and
4 transport to the detection subsystem the reaction units from a selected one of the at least one
5 discrete reaction platform independently of any other discrete reaction platform.
- 1 5. The system according to claim 4 wherein said gripping mechanism
2 comprises a movable arm rotatable about an axis perpendicular to a work field of the reaction
3 platform.
- 1 6. The system according to claim 4 further including:

2 a fluidics subsystem for storing detection and processing reagents and for
3 transferring the detection and processing reagents to the flow cells.

1 7. The system according to claim 4 wherein a plurality of the reaction
2 platforms are disposed side by side adjacent one another relative to the detection subsystem.

1 8. The system according to claim 4 wherein a plurality of the reaction
2 platforms are disposed front to back adjacent one another relative to the detection subsystem.

1 9. The system according to claim 4 wherein the at least one reaction
2 platform is operative to prepare the nucleic acid samples as fluorescent sequencing reaction
3 products for optical observation, and wherein

4 the detection subsystem is operative to capturing color images of the plurality
5 of fluorescent reaction products for computer-aided identification.

1 10. A method for processing and detecting an automated sequencing
2 reaction on a nucleic acid comprising:

3 placing a plurality of flow cells on a reaction platform, each flow cell
4 comprising a plurality of distinguishable reaction sites and a plurality of nucleic acid samples
5 attached to the plurality of reaction sites;

6 injecting a processing reagent into the flow cells;

7 reacting the processing reagent with the nucleic acid samples for a processing
8 period to invoke sequencing reactions producing fluorescent sequencing products; thereafter

9 transferring the flow cells from the reaction platform to a detection subsystem
10 using an automated coupling subsystem that is physically loosely coupled to the detection
11 subsystem;

12 illuminating the flow cells at the detection subsystem to cause the fluorescent
13 sequencing products to fluoresce in distinguishable spectra at the distinguishable reaction
14 sites; and

15 capturing a color image of fluorescence from the distinguishable reaction sites
16 in the flow cells for use to identify nucleic acid sequences, where duration of the capturing
17 step is substantially less than the reacting step.

CLAIMS

1. An automated assembly for sequencing nucleic acids, comprising:
 - a reaction subsystem comprising one or more flow cells on a reaction platform, the one or more flow cells being configured for carrying out biochemical sequencing reactions on nucleic acid samples;
 - an imaging subsystem configured for capturing optical images of a flow cell from said one or more flow cells when present in the imaging subsystem;
 - a carrying device configured for transferring any of the one or more flow cells on the reaction platform to and from the imaging subsystem;
 - wherein the reaction subsystem and the imaging subsystem are configured to operate independently at different rates, and
 - wherein the assembly further comprises shock isolators that are constructed and arranged so as to sufficiently isolate the imaging subsystem from vibrations from the carrying device.
2. The assembly of claim 1, wherein more than one flow cells are situated on the reaction platform.
3. The assembly of either claim 1 or claim 2, wherein the reaction subsystem comprises two or more reaction platforms.
4. The assembly of any of claims 1 to 3, wherein the imaging subsystem comprises a CCD (charged coupled device).
5. The assembly of any of claims 1 to 4, wherein the imaging subsystem is configured to detect 6 to 8 different colors.
6. The assembly of any of claims 1 to 5, wherein the imaging subsystem is configured so that the number of pixels per nucleic acid molecule can be adjusted by increasing or decreasing the field of view of an objective lens, for example, from 10 pixels per nucleic acid molecule to 2.5 pixels per nucleic acid molecule.
7. The assembly of any of claims 1 to 6, wherein the carrying device comprises a control and sensing mechanism and the imaging subsystem comprises a position registration mechanism.
8. The assembly of any of claims 1 to 7, wherein the imaging subsystem includes a camera having a resolution of 10 to 16 megapixels.
9. The assembly of claim 8, wherein the camera includes a CCD detector having an exposure time of about 300 milliseconds.
10. The assembly of any of claims 1 to 9, wherein each of the one or more flow cells comprises a sealed chamber with a volume of between 50 μ L and 300 μ L.
11. The assembly of any of claims 1 to 10, wherein the one or more flow cells on the reaction platform each contains an array of fluorescently labeled nucleic acids.

12. The assembly of any of claims 1 to 11, further comprising a computer programmed to coordinately control operation of the reaction subsystem, the detection subsystem, and the carrying device.
13. An automated assembly for sequencing nucleic acids, comprising:
 - a reaction subsystem that is configured to support and operate a plurality of flow cells that each carry out biochemical sequencing reactions on an array of nucleic acids;
 - an imaging subsystem configured for capturing optical images of the flow cells when present in the imaging subsystem;
 - a carrying device configured for transferring a flow cell between the reaction subsystem and the detection subsystem; and
 - shock isolators that are constructed and arranged so as to sufficiently isolate the imaging subsystem from vibrations from the reaction subsystem and from the carrying device, so that the vibrations do not disrupt image capture by the imaging subsystem.
14. The assembly of claim 13, further comprising a computer programmed to coordinately control operation of the reaction subsystem, the detection subsystem, and the carrying device.
15. The assembly of either claim 13 or claim 14, wherein the carrying device comprises a motorized gripping mechanism.
16. The assembly of any of claims 13 to 15, wherein the carrying device comprises a control and sensing mechanism that regulates transfer of flow cells by the carrying device so as to prevent vibrations during transfer.
17. The assembly of any of claims 1 to 16, wherein the imaging subsystem comprises a position registration mechanism.
18. The assembly any of claims 1 to 17, wherein the reaction subsystem comprises a number of reservoirs of processing fluids attached to a pumping mechanism.
19. The assembly of any of claims 1 to 18, with a plurality of flow cells on a reaction platform in the reaction subsystem, each flow cell comprising a plurality of distinguishable reaction sites.
20. The assembly of any of claims 1 to 19, with nucleic acids or primers attached to surface regions in the flow cells.
21. The assembly of any of claims 1 to 20, wherein each of the flow cells contains a sealed chamber with a volume of between 50 μ L and 300 μ L.