CLAIMS

What is claimed is:

1. A device for base calling, comprising:

a biosensor and a receptacle configured to hold the biosensor, the biosensor having

a sample surface including pixel areas and is configured to hold a plurality of clusters during a sequence of sampling events such that the clusters are distributed unevenly over the pixel areas,

an array of sensors, where each sensor in the array is configured to sense information from one or more clusters disposed in corresponding pixel areas of the sample surface to generate a pixel signal in a sampling event, the array configured to generate the plurality of sequences of pixel signals, the array having a number N of active sensors, the sensors in the array disposed relative to the sample surface to generate respective pixel signals during the sequence of sampling events from the number N of corresponding pixel areas of the sample surface to produce the plurality of sequences of pixel signals, and

a communication port which is configured to output the plurality of sequences of pixel signals; and

a signal processor coupled to the receptacle, and configured to execute time sequence and spatial analysis of the plurality of sequences of pixel signals to detect patterns of illumination corresponding to a number N + M of individual clusters on the sample surface from the number N of active sensors, where M is a positive integer, to classify the results of the sequence of sampling events for the number N + M of individual clusters, and is configured to use the plurality of sequences of pixel signals gathered from a group of the pixel areas on which at least two clusters are unevenly distributed to determine spatial characteristics of the at least two clusters, including location of the at least two clusters on the sample surface, wherein the plurality of sequences of pixel signals encodes differential crosstalk between the at least two clusters resulting from their uneven distribution over the group of pixel areas.

2. A device for base calling, comprising:

a biosensor having a sample surface including pixel areas and an array of wells overlying the pixel areas, the biosensor including two equal-sized wells and two clusters per pixel area, the two equal-sized wells per pixel area including a dominant well and a subordinate well, the dominant well having a larger cross section over an active area of the pixel area than the subordinate well.

3. The device of claim 2, wherein the biosensor includes

the array configured to generate a plurality of sequences of pixel signals, the array having a number N of active sensors, the sensors in the array disposed relative to the sample surface to generate respective pixel signals during the sequence of sampling events from the number N of corresponding pixel areas of the sample surface to produce the plurality of sequences of pixel signals, and

a communication port which is configured to output the plurality of sequences of pixel signals.

4. The device of claim 2, wherein the two equal-sized wells have different offsets relative to a center of the pixel area.

5. The device of claim 4, wherein, during a sampling event, the pixel area is configured to receive different amounts of illumination from the two equal-sized wells, and

wherein the pixel signal for each sampling event in at least one sequence of pixel signals in the plurality of sequences of pixel signals represents sensed information from the two clusters in the corresponding pixel area.

6. The device of claim 5, wherein each of the two equal-sized wells is configured to hold at least one cluster during the sampling event.

7. The device of claim 6, wherein, during the sampling event, the pixel area is configured to receive an amount of illumination from a bright cluster in the dominant well that is greater than an amount of illumination received from a dim cluster in the subordinate well.

8. The device of claim 7, wherein the biosensor is coupled to signal processor, the signal processor configured to receive and to process the plurality of sequences of pixel signals to identify bases present in a number N + M of clusters from the number N of active sensors, including for the bright and dim cluster

mapping into at least four bins a first pixel signal generated by a sensor corresponding to the pixel area during a first illumination stage of the sampling event,

mapping into at least four bins a second pixel signal generated by the sensor during a second illumination stage of the sampling event, and

logically combining the mapping of the first and second pixel signals to identify the bases present in the bright cluster and the dim cluster.

9. A device for base calling, comprising:

a biosensor having a sample surface including pixel areas and an array of wells overlying the pixel areas, with at least two clusters per pixel area; and

an illumination system that is coupled to the biosensor and that is configured to illuminate the pixel areas with different angles of illumination during a sequence of sampling events, including, for a sampling event in the sequence of sampling events, to illuminate each of the wells with off-axis illumination to produce asymmetrically illuminated well regions in each of the wells.

10. The device of claim 9, wherein the biosensor includes

an array of sensors, where each sensor in the array is configured to sense information from the at least two clusters disposed in corresponding pixel areas of the sample surface to generate a pixel signal in a sampling event, the array configured to generate a plurality of sequences of pixel signals, the array having a number N of active sensors, the sensors in the array disposed relative to the sample surface to generate respective pixel signals during the sequence of sampling events from the number N of corresponding pixel areas of the sample surface to produce the plurality of sequences of pixel signals, and

a communication port which is configured to output the plurality of sequences of pixel signals.

11. The device of claim 9, wherein the asymmetrically illuminated regions of a well include at least a dominant well region and a subordinate well region, such that during the sampling event the dominant well region is illuminated more than the subordinate well region.

12. The device of claim 11, wherein the well holds more than one cluster during the sampling event, with the dominant and subordinate well regions each including a cluster.

13. The device of claim 12, wherein, during the sampling event, a pixel area overlying the well receives an amount of illumination from a bright cluster in the dominant well region that is greater than an amount of illumination received from a dim cluster in the subordinate well region.

14. The device of claim 13, further comprising a signal processor, wherein the biosensor is coupled to the signal processor, the signal processor configured to receive and to process the plurality of sequences of pixel signals to identify bases present in a number N + M of clusters from the number N of active sensors, including for the bright and dim cluster

mapping into at least four bins a first pixel signal generated by a sensor corresponding to the pixel area during a first illumination stage of the sampling event,

mapping into at least four bins a second pixel signal generated by the sensor during a second illumination stage of the sampling event, and

logically combining the mapping of the first and second pixel signals to identify the bases present in the bright cluster and the dim cluster.

15. The device of claim 9, wherein the off-axis illumination is at a forty-five degree angle.

16. The device of claim 9, wherein one well overlies per pixel area.

17. The device of claim 9, wherein two wells overlie per pixel area.