

CLAIMS

[Claim 1]. A computer-implemented method of base calling, the method including:
accessing an image whose pixels depict intensity emissions from a target cluster and intensity emissions from additional adjacent clusters;
selecting a lookup table, ~~based on a subpixel location of a target cluster center within a pixel,~~ that contains pixel coefficients that are configured to maximize a signal-to-noise ratio;
convolving the pixel coefficients with intensity values of the pixels in the image to produce an output; and
base calling the target cluster based on the output;
~~wherein the pixel coefficients of the selected lookup table are trained using as ground truth target intensities in intensity profiles of images that were reliably base called for target clusters.~~

[Claim 2]. The computer-implemented method of claim 1, wherein the signal maximized in the signal-to-noise ratio is the intensity emissions from the target cluster, and the noise minimized in the signal-to-noise ratio is the intensity emissions from the adjacent clusters, plus additional noise sources.

[Claim 3]. The computer-implemented method of claim 1, wherein the pixels include a center pixel that contains ~~the~~a center of the target cluster, and each pixel in the pixels is divisible into a plurality of subpixels.

[Claim 4]. The computer-implemented method of claim 3, wherein the lookup table is a subpixel lookup table.

[Claim 5]. The computer-implemented method of claim 4, further including:
depending upon a particular subpixel, in a plurality of subpixels of the center pixel, which contains the center of the target cluster, selecting, from a bank of subpixel lookup tables, the subpixel lookup table that corresponds to the particular subpixel, the selected subpixel lookup table containing the pixel coefficients;
element-wise multiplying the pixel coefficients to the intensity values of the pixels in the image and summing products of the multiplications to produce the output, the pixel coefficients serving as weights and the output being a weighted sum of the intensity values; and

using the output to base call the target cluster, including generating the output for each imaging channel in a plurality of imaging channels and base calling the target cluster using the output for each imaging channel.

[Claim 6]. The computer-implemented method of claim 5, wherein the element-wise multiplication adds a bias for given set of equalizer coefficients, wherein the bias is a DC offset that averages background noise intensity.

[Claim 7]. The computer-implemented method of claim 5, further including:
selecting additional subpixel lookup tables, from the bank of subpixel look tables, which correspond to subpixels that are contiguously adjacent to the particular subpixel;
generating, based on pixel coefficients of the selected subpixel lookup table and the selected additional subpixel lookup tables, interpolated pixel coefficients that are configured to maximize the signal-to-noise ratio;
convolving the interpolated pixel coefficients with the intensity values of the pixels in the image to produce an output; and
base calling the target cluster based on the output.

[Claim 8]. The computer-implemented method of claim 7, further including:
element-wise multiplying the interpolated pixel coefficients to the intensity values of the pixels in the image and summing products of the multiplications to produce the output, the interpolated pixel coefficients serving as weights and the output being a weighted sum of the intensity values.

[Claim 9]. The computer-implemented method of claim 1, further including training an equalizer using at least one of least squares estimation, ordinary least squares, least-mean squares, and recursive least-squares to generate the pixel coefficients.

[Claim 10]. The computer-implemented method of claim 9, further including training the equalizer in an offline mode in which the pixel coefficients of subpixel lookup tables are fixed after being trained on batches of training data from a previously executed sequencing run.

[Claim 11]. The computer-implemented method of claim 10, further including training the equalizer in an online mode in which the pixel coefficients of subpixel lookup tables are iteratively updated during an ongoing sequencing run.

[Claim 12]. The computer-implemented method of claim 11, further including accessing base-wise intensity distributions of each of ~~the~~ four bases A, C, G, and T generated during prior base calling of images in the training data, selecting respective centers of the base-wise intensity distributions as base-wise ground truth target intensities for corresponding color channels, and using the base-wise ground truth target intensities to train the equalizer.

[Claim 13]. The computer-implemented method of claim 12, further including pre-training the equalizer in the offline mode and retraining the equalizer in the online mode.

[Claim 14]. The computer-implemented method of claim 9, further including generating the lookup tables in a bank of subpixel lookup tables by together applying a single set of equalizer coefficients and a precalculated set of interpolation filters, including interpolating pixel intensities to generate inputs for the equalizer.

[Claim 15]. The computer-implemented method of claim 1, further including making ~~the~~ a center of the target cluster concentric with a center of ~~the~~ a center pixel by:
registering the image against a template image and determining affine transformation and nonlinear transformation parameters;
using the affine transformation and nonlinear transformation parameters to transform location coordinates of the target cluster and the additional adjacent clusters to image coordinates of the image and generating a transformed image with transformed pixels; and
applying interpolation using the transformed location coordinates of the target cluster and the additional adjacent clusters to make their respective cluster centers concentric with centers of respective transformed pixels that contain the cluster centers.

[Claim 16]. A non-transitory computer readable storage medium impressed with computer program instructions to perform base calling, the instructions, when executed on a processor, implement actions ~~method~~ comprising:
accessing an image whose pixels depict intensity emissions from a target cluster and intensity emissions from additional adjacent clusters;
selecting a lookup table, ~~based on a subpixel location of a target cluster center within a pixel,~~ that contains pixel coefficients that are configured to maximize a signal-to-noise ratio;
convolving the pixel coefficients with intensity values of the pixels in the image to produce an output; and

base calling the target cluster based on the output;

~~wherein the pixel coefficients of the selected lookup table are trained using as ground truth target intensities in intensity profiles of images that were reliably base called for target clusters.~~

[Claim 17]. The non-transitory computer readable storage medium of claim 16, wherein the signal maximized in the signal-to-noise ratio is the intensity emissions from the target cluster, and the noise minimized in the signal-to-noise ratio is the intensity emissions from the adjacent clusters, plus additional noise sources.

[Claim 18]. The non-transitory computer readable storage medium of claim 16, implementing the ~~method actions~~ further comprising training an equalizer using at least one of least squares estimation, ordinary least squares, least-mean squares, and recursive least-squares to generate the pixel coefficients.

[Claim 19]. A system including one or more processors coupled to memory, the memory loaded with computer instructions to perform base calling, the computer instructions, when executed on the one or more processors, implement actions comprising:

accessing an image whose pixels depict intensity emissions from a target cluster and intensity emissions from additional adjacent clusters;

selecting a lookup table, ~~based on a subpixel location of a target cluster center within a pixel,~~ that contains pixel coefficients that are configured to maximize a signal-to-noise ratio;

convolving the pixel coefficients with intensity values of the pixels in the image to produce an output; and

base calling the target cluster based on the output;

~~wherein the pixel coefficients of the selected lookup table are trained using as ground truth target intensities in intensity profiles of images that were reliably base called for target clusters.~~

[Claim 20]. The system of claim 19, further implementing actions comprising training an equalizer using at least one of least squares estimation, ordinary least squares, least-mean squares, and recursive least-squares to generate the pixel coefficients.