for a given structure, the nearest neighbor distances (NNDs) decrease. Calculated average NNDs for our simulated mitochondria data ranged from 51.3 nm (n=100) to 11.2 (n=2,000). Comparing the average NND values to the determined drift correction precision confirms a linear relationship between the two measures. Statistical arguments further indicate that doubling n while maintaining the average NND and local structural features (for example by imaging two identical structures next to each other) results in $\sqrt{2}$-fold drift compensation improvement.

In practical applications, as demonstrated for diverse samples represented by the simulated structures, the described cross-correlation technique can correct drift of several hundred nanometers to values below 5 nm. This is achieved for typical localization precision values and requires only several hundred to 2,000 localized molecules for each time interval. Our method requires no fiduciary markers and is straightforward to implement. We believe that this technique can easily be applied in a wide variety of super-resolution microscopes.

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