

Supplementary information:

A typical cell in the bright field mode is shown in Figure S1(a). The PWS system acquires a three dimensional data cube $I(x,y,\lambda)$ for each pixel (x,y) in the cell image. Three different pixels (1 pixel $\sim 100\text{nm} \times 100\text{nm}$ area within the cell) within the cell is shown as an example in Figure S1(a)(Blue, green and red cross). Figure S2(b) shows the normalized spectrum $R(\lambda)$ from three different pixels within a cell. $R(\lambda)$ for each pixel (x,y) is obtained as follows: First, the spectrum $I(x,y, \lambda)$ is normalized (normalized with the incident light) and filtered with a low pass filter (6th order Butterworth filter with a normalized cutoff frequency of 0.08). Second, a low order polynomial ($I_p(\lambda)$) due to instrument artifact is removed from the original spectrum. Thus for each pixel (x,y) we get, $R(\lambda) = I(\lambda) - I_p(\lambda)$. From each spectrum $R(\lambda)$, $\langle R \rangle$ is calculated as the root-mean square average of $R(\lambda)$. $\langle R \rangle$ can be theoretically written as follows(1):

$$\langle R \rangle \approx \frac{2k^2 L_d L}{n_0^2}$$

where k is the wave number ($k = 2\pi/\lambda$), L is the thickness of the cell and n_0 is the average refractive index of the cell (n_0 is a constant ~ 1.38).

Next, the autocorrelation function $C(\Delta k)$ from the spectrum $R(k)$ is calculated as follows: $C(\Delta k) = \langle R(k) * R(k + \Delta k) \rangle / \langle R(k)R(k) \rangle$. $C(\Delta k)$ can be theoretically written as follows:

$$\ln(C(\Delta k)) = -B L * (\Delta k)^2$$

where B is a constant(1). A typical $\ln(C(\Delta k))$ vs $(\Delta k)^2$ for a particular pixel (x,y) is shown in Figure S1(c). Thus by knowing $R(\lambda)$ and $C(\Delta k)$ for each pixel in a cell, L_d can be calculated for each pixel (x,y) as follows:

$$L_d = \frac{B \langle R \rangle}{2k^2} \frac{(\Delta k)^2}{-\ln(C(\Delta k))} \Big|_{\Delta k \rightarrow 0}$$

The L_d value thus calculated for each pixel (x,y) within the cell is shown in Figure S1(d).

Supplementary Figure Legend:

Figure S1: Steps for calculating disorder strength (L_d) using PWS system: (a) A typical cell in the bright field mode with three different pixels marked in the image (Blue, green and red cross). (b) The normalized spectrum $R(\lambda)$ from three different pixels within the cell. (c) A typical autocorrelation decay ($C(\Delta k)$) obtained from $R(k)$. The

autocorrelation slope ($\frac{\ln(C(\Delta k))}{(\Delta k)^2}$) is obtained by fitting a linear polynomial (solid line) to

the logarithm of the autocorrelation function $(\ln(C(r)))$ (circles). (d) The 2D disorder strength map obtained by calculating L_d for each pixel (x,y) in the cell. From these 2D images, the mean intracellular disorder strength of an individual cell is obtained.

1. Subramanian, H., Pradhan, P., Liu, Y., Capoglu, I. R., Li, X., Rogers, J. D., Heifetz, A., Kunte, D., Roy, H. K., Taflove, A., and Backman, V. Optical methodology for detecting histologically unapparent nanoscale consequences of genetic alterations in biological cells. Proc Natl Acad Sci U S A, 2008.