Abstract: This work describes the use of computational optics principles to first encode the specimen signal information optically using specially-engineered point spread functions (PSFs), next record the information using the microscope's CCD detector, and then decode the signal using custom nonlinear processing algorithms. The significance of this approach is the PSFs are designed in such a way that the signals of interest can be easily separated from the system noise. This overcomes a common problem that is frequently encountered in biological microscopy, that of image degradation and loss of detail due to the presence of noise. Results demonstrate that this approach can greatly improve a microscope's imaging capabilities by reducing the noise and reconstruction artifacts often present in photon-starved applications such as live-cell fluorescence, object tracking and extended depth of field imaging.