PHYSICAL LIMITS TO SPATIAL RESOLUTION OF OPTICAL RECORDING: PHOTON SCATTER AND OPTICAL DEFOCUS*†

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Abstract

Although optical imaging "resolution" is sometimes claimed to be as small as $50\ \mu\mathrm{m}$, the spatial resolution of optical imaging has received little experimental study. However, there is a fundamental physical limit to the point-spread function (PSF) determined by the scattering of photons in cortex. Three constants determine the spatial distribution of scattered light in gray (white) matter: [1] the absorption coefficient $\mu_a = 2.7\ (2.2)\ \mathrm{cm}^{-1}$, [2] the scattering coefficient $\mu_s = 354\ (532)\ \mathrm{cm}^{-1}$, [3] the scattering anisotropy coefficient $g = 0.94\ (0.82)$. Imaging system optics also contribute blur that is convolved with the photon probability distribution. Orbach and Cohen (*J. Neurosci.*, 3:2251–62, 1983) measured the cortical PSF by imaging a pinhole in aluminum foil through $500\ \mu\mathrm{m}$ of resected salamander cortex with microscope optics, reporting a PSF of $200\ \mu\mathrm{m}$ FWHM. To adjust this measurement for an *in-vivo* point source with macroscope optics (which have considerably broader defocusing) and backscatter from depths below the aperture, we performed a Monte Carlo simulation of photon scatter. Our simulation, which included a diffractive optics model ($\lambda = 633\ \mathrm{nm}$) for a macroscope focused at $300\ \mu\mathrm{m}$ below the cortical surface, **produced a PSF of** $235\ \mu\mathrm{m}$ **FWHM (Cauchy distribution, equivalent to** $> 300\ \mu\mathrm{m}$ **Gaussian)** for a vertical line, or *columnar*, source with cortical depth from 200 to $500\ \mu\mathrm{m}$. This result is in rough agreement with the measurement of Orbach and Cohen after our adjustment to include the missing backscatter and macroscope optics. These results contradict estimates of spatial resolution of optical imaging in the range of 50–100 $\mu\mathrm{m}$ (Bonhoeffer and Grinvald, *J. Neurosci.*, 13:4157–80, 1993). The consequences of this result for current models of cortical functional architecture are discussed in a companion abstract (Schwartz et al., *Soc. Neuro. Abs.*, 2003).

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