BILOGICAL IMAGING FROM THE MACRO TO NANOSCALE

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Biology offers different information at different scales: tissues show their physiology, cells show their form, and molecules show their organization. To study health and disease, we need optical tools suited to each scale and ways to combine their measurements into a clear picture. This presentation describes imaging methods we are developing to overcome limits in resolution, speed, and scattering, with the aim of improving diagnosis, assessing drug response, and uncovering the biological mechanisms that shape health and disease.

At the **macroscopic scale**, Spatial Frequency Domain Imaging and polarization imaging provide quantitative, label-free maps of tissue absorption, scattering, and structural order. These methods measure key physiological signals such as hemoglobin concentration, oxygen saturation, and melanin content, and they allow noninvasive evaluation of perfusion, wound depth, inflammation, and pressure-injury risk. Because they work without contact and can cover large areas quickly, they are well suited for clinical studies, point-of-care use, and population-level screening.

At the **microscopic scale**, biological imaging faces major challenges. Scattering limits penetration depth, confocal scanning limits imaging speed, and tissue motion disrupts volumetric imaging. To address these problems, we examine the strengths and weaknesses of confocal, widefield, and light-sheet methods, and we introduce a three-dimensional confocal cavity array that captures several optical sections at once. This design increases volumetric imaging speed by a factor of ten and offers a practical route to real-time, depth-resolved cellular imaging in living tissue. These advances may support intraoperative pathology, dermatological assessment, and rapid diagnosis without the need for physical biopsies.

At the **nanoscale**, super-resolution imaging reveals nano-morphology beyond diffraction limited microscopy. We outline the principles of some super-resolution techniques and introduce a new system we are developing that records three-dimensional position, emission spectrum, and dipole orientation from each single-molecule event. The ability to collect these signals at once yields a more complete picture of molecular structure, environment, and dynamics. We aim to apply this capability to endogenous chromatin and related structures in order to identify early optical signatures of carcinogenesis.

Together, these technologies create a multi-scale imaging framework that links molecular events to cellular behavior and to tissue-level changes. This integration can support earlier diagnosis, improve the monitoring of treatment, and guide the development of new optical tools for both biomedical and materials research.