Pupil Phase Series: A Fast, Accurate, and Energy-Conserving Model for Forward and Inverse Light Scattering in Thick Biological Samples

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We present the pupil phase series (PPS), a fast and accurate forward scattering algorithm for simulating and inverting multiple light scattering in large biological samples. PPS achieves high-angle scattering accuracy and energy conservation simultaneously by introducing a spatially varying phase modulation in the pupil plane. By expanding the scattering term into a Taylor series, PPS achieves high precision while maintaining computational efficiency. We integrate PPS into a quasi-Newton inverse solver to reconstruct the three-dimensional refractive index of a 180 μm-thick human organoid. Compared to linear reconstruction, our method recovers subcellular features—such as nuclei and vesicular structures—deep within the sample volume. PPS offers a scalable and interpretable alternative to conventional solvers, paving the way for high-throughput, label-free imaging of optically thick biological tissues.

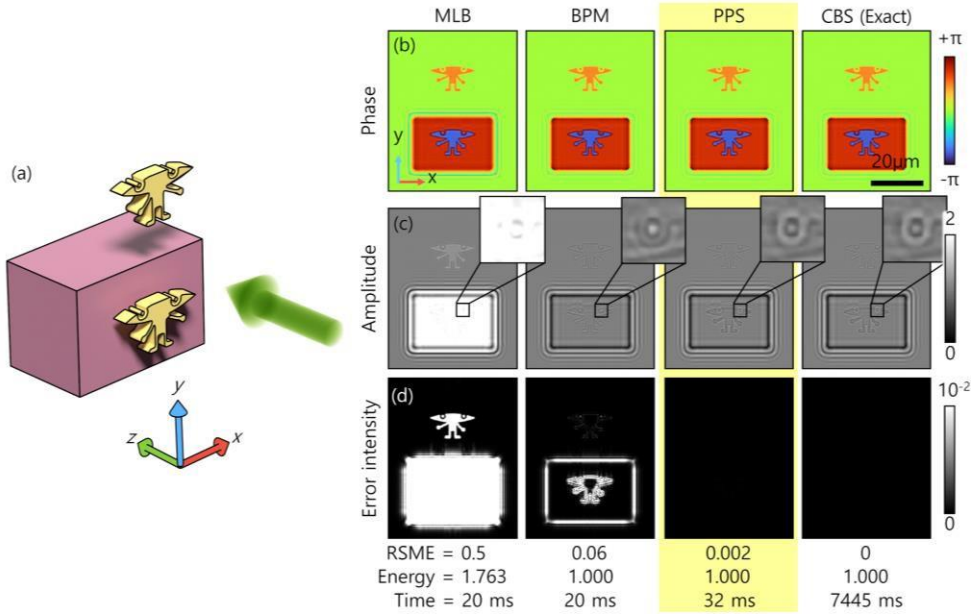

Fig. 1. Scattering simulation benchmarking. a) 3D scattering simulation layout. The green arrow shows the direction of illumination. Cuboid scatterer (pink color) and phase target (yellow color). b) Transmitted phase and b) amplitude for different simulation methods. d) Error intensity image in comparison with the CBS method e) Benchmarking of root mean square error , transmitted energy (mean intensity) and execution time.