OPTIMIZING FIELD-OF-VIEW OF DEEP-TISSUE SCANNING MICROSCOPY

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For centuries, the optical microscope has been a crucial instrument for new biological findings, as microscopes were the first devices allowing to observe the internal processes of the cell. Unfortunately, this observation requires the use of thin samples, as biological tissue scatters the incoming light, resulting in a blurred image. An ever increasing number of deep-tissue imaging technique have pushed the penetration depth of the optical microscope. Methods such as adaptive optics [1] allow focusing inside biological tissue by correcting for scattering introduced by the sample. However, adaptive optics methods can only correct for image distortions caused by scattering over a single small area (i.e., field-of-view) within tissue.

The field-of-view is dictated by the wave correlations present in the scattering medium. The well-known "optical memory effect" [2] and a more recent "anisotropic memory effect" [3] are two wave correlations that offer different methods to optimize adaptive optics systems. Nevertheless, the best strategy is to enlarge their imaging field-of-view is still unknown. Therefore, we have studied the memory effects inside tissue-like samples. We found that the two memory effects are mere manifestations of a more general source of wave correlations. We developed a theoretical model to describe this new generalized memory effect and found that an ideal combination of tilting and shifting of the incident beam exist, which allows the field of view of an AO system to be improved. In Figure 1, we illustrate how the three different memory effect can be used for focus scanning.

Our new framework also provides the *optimal* mechanism to form as large a field-of-view as possible when using adaptive optics and other deep-tissue imaging techniques. Our new memory effect can thus be used to obtain clear microscope images from deep within tissue, enabling observations of cellular processes within the cell's natural habitat.

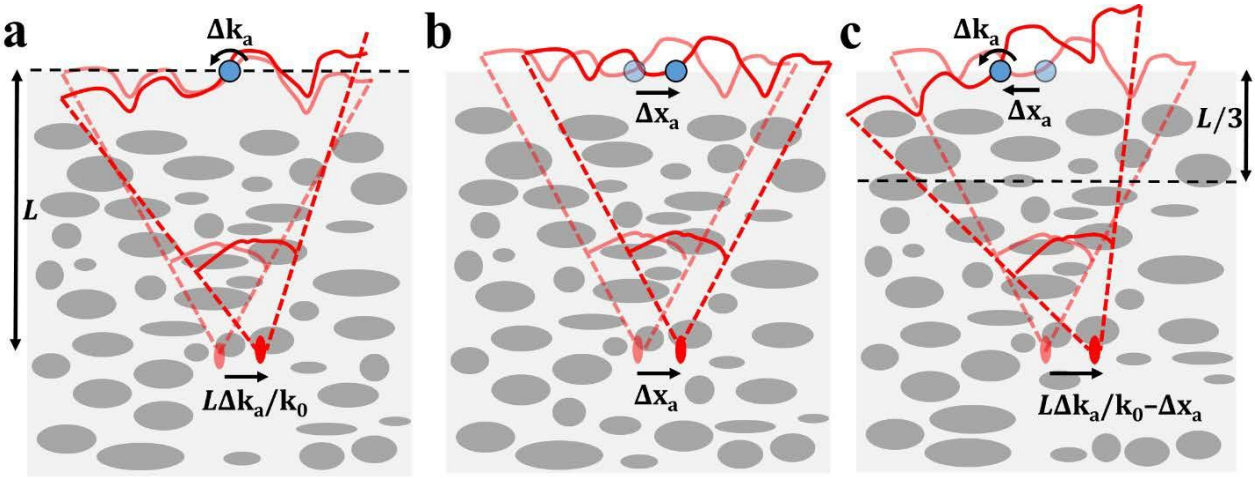

Figure 1 - Comparison of the three different memory effect for focus scanning in terms of tilting delta_ka and shifting delta_xa at the sample surface. a) The optical memory effect [2]. b) The anisotropic memory effect [3]. c) The generalized memory effect.

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