

Optical recording of cell electrical activity by Digital Holographic Microscopy

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One of the most appealing applications of digital holographic microscopy DHM in the field of live sciences is related to its ability in imaging marker free transparent living specimen thanks to its capacity to accurately and quantitatively measure the phase of the detected light, from a single recorded hologram [1].

Basically, the phase shift induced by transparent specimen, called also phase object, on the transmitted wavefront contains information about both the cell morphology (cell volume and shape) and the intracellular refractive index. Previous dynamics studies with DHM have shown that the impact of the refractive index is a stronger determinant of the value of the phase than the volume changes [2]. We have determined that the intracellular refractive index is highly dependent on the concentration of the cell proteins. Thus, an entry of water (accompanying the transmembrane movement of ions) will dilute the intracellular protein content resulting in a decrease in the phase while an exit of water will lead to a phase increase.

Against this background, we have analyzed the optical signal detected by DHM associated to the chloride flux triggered by GABA application to a neuronal GABA_A receptor-expressing Human Embryonic Kidney (HEK) cells. We have combined patch clamp recordings and DMH in the same cells following GABA application. We have observed a phase shift in the optical signal detected by DHM after application of GABA (3 μ M, 30s) for a holding potential to -100mV. Furthermore, the value for the reversal potential for chloride obtained by establishing phase/voltage relations (ϕ/V) is superimposable to that obtained by voltage/current relations (I/V); this experimentally-determined reversal potential is dependent on the intracellular concentration of chloride. Finally, there is a mathematical correlation between the phase signal and the recorded current triggered by GABA, allowing a prediction of the actual current by a simple analysis of phase shift. These data indicate that the quantitative monitoring of the DHM phase signal affords the possibility to analyze at the single-cell level with a simple and non-invasive optical method the effect of neurotransmitter-receptor activations known to result in excitability changes.

References

[1] P. Marquet et al., "Digital holographic microscopy: a noninvasive contrast imaging technique allowing quantitative visualisation of living cells with subwavelength axial accuracy." *Optics letters* **30**(5): 468-70 (2005).

[2] Rappaz, B., et al., "Measurement of the integral refractive index and dynamic cell morphometry of living cells with digital holographic microscopy." *Optics Express* **13**(23): 9361-9373 (2005).