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Centre de Neurosciences Psychiatriques

CNP SEMINAR

ANNOUNCEMENT

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“New tools to probe the brain with light”

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The future of neuroscience lies in our ability to assess, in a context sensitive manner, how each component of the enormously complex CNS integrates, processes and transfers neurochemical information. Although colossal advances in understanding cell signalling events have been made using *ex vivo* preparations, the highly reactive and plastic CNS imposes *in vivo* studies to assess their relevance to normal function and pathology. Thus, the true enabling discovery technologies will be those that bridge single cell molecular signalling studies with whole animal physiological and behavioural assessments. The recent advent of photoactivatable proteins to generate novel sensors and actuators open new arrays of possibilities on this front. Yet, harnessing their full potential remains limited by properties of light such as diffraction, absorption and scattering which restrict resolution and depth of observation/intervention. Thus, our ability to probe and control cellular and molecular events across the length and time scales (from subcellular compartments to neuronal networks; from milliseconds to days) *in vivo* hinges on the development of novel techniques to deliver light and measure events with extreme sensitivity and precision.

I will describe recent techniques developed at the *Neurophotonics Centre* in Quebec City (www.neurophotonics.ca) to undertake these challenges. At one end of the spectrum, to conduct quantitative analysis of molecular interactions *in situ*, we developed an image analysis technique entitled spatial intensity distribution analysis (SpIDA). It can be applied to analysis of single images and thus chemically fixed tissue as well as live cells and yields accurate measurements of densities and oligomerization states *in situ* at previously unachievable levels. At the other end of the spectrum, to enable single cell signalling and electrophysiology studies in deep brain structures, we developed a dual-core fibre optics-based microprobe, with an optical core to locally excite and collect fluorescence and an electrolyte-filled hollow core for extracellular single unit electrophysiology. The probe can detect single fluorescent cells, combine electrical and optical Ca²⁺ measurements from single neurons, and serve for optogenetic activation of single neurons, vastly expanding possibilities for *in vivo* electrophysiology with access to single cell molecular technologies.

Useful recent publications:

1. Godin, A.G., Costantino, S., Lorenzo, L.-E., Swift, J.L., Sergeev, M., Ribeiro-da-Silva, A., De Koninck, Y. & Wiseman, P.W. (2011) Revealing protein oligomerization and densities *in situ* using Spatial Intensity Distribution Analysis. *Proc. Natl. Acad. Sci. USA* 108:7010-7015.
2. LeChasseur, Y., Dufour, S., Lavertu, G., Bories, C., Deschênes, M., Vallée, R. & De Koninck, Y. (2011) A microprobe for parallel optical and electrical recordings from single neurons *in vivo*. *Nat. Methods* 8:319-325.
3. Bélanger, E., Crépeau, J., Laffray, S., Vallée, R., De Koninck, Y. & Côté, D. (2012) Live animal myelin histomorphometry of the spinal cord with video-rate multimodal nonlinear microendoscopy. *J. Biomed. Opt.* 17:021107.