New approaches for remote, contact-less control of stimulatory cells in-vivo

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We are interested in communicating wirelessly with specifically selected cells in-vivo, in especially with neurons or other excitable cells. Our motivation ranges from fundamental neuroscience analysis of neuro-circuitry to biomedical applications.

Currently, the most successful methods for wireless communication between engineered systems and cells rely on visible light to transmit the information. During the past two decades, the optical read-out of cellular signals has been perfected. Today, an array of fluorescent sensors for biological signals is available. Recently, the optical stimulation of cells was also pushed to a practical level by the development of optical activatible ion-channels. In cell culture, the optical communication seems optimal because of its speed of information transfer and the ease of application. However, the inability of visible light to penetrate tissue means that for many in-vivo applications the light has to be delivered via optical fiber.

In contrast magnetic fields penetrate tissue without attenuation. Therefore we focus our efforts on developing remote in-vivo stimulation using magnetic fields. Currently, remote magnetic and electrical field stimulation methods, relying on endogenous sensitivity of cells to electrical fields, are indirect methods not targeted to specific cells. Recently, two approaches proposed using super-paramagnetic nanoparticles as signal transducer and to target these to specific cells. Kumar et al induced aggregation of super-paramagnetic nanoparticles in field gradients to induce receptor aggregation and subsequently cell signaling; we used local heating around super-paramagnetic nanoparticles in oscillatory magnetic to open temperature sensitive ion channels and sequent cell signaling. We consider local heating as particularly promising for in-vivo applications because it does not require any complex geometry, the field strength and frequencies are similar to fields used in MRI instruments, and animals may move freely within the magnetic field. By combining super-paramagnetic nanoparticle heating with temperature sensitive ion channels, we demonstrated in cell culture that cells and neurons may be activated, and then in-vivo that the behavior of nematodes may be influenced.

This local heating approach faces still several challenges. Currently it takes about 5 s to activate specific cells. To study neuro-transmission, or use this approach in biomedical applications, the heat delivery to the ion channel has to be optimized to accelerate the signal transmission at least ten-fold, ideally 100-fold. Furthermore, optimization of the nanoparticle stability on the cells is required for continuous and repeated stimulation over days. In addition, to avoid overheating of the membrane, a temperature feedback should be included. Applying this approach in neuroscience, which is our motivation, will also require developing in vivo targeting to the brain across the blood brain barrier. However, the current approach already provides a useful in-vivo method for wireless stimulation of slower processes outside of the brain.