Karolinska Institutet

Institutionen för Neurovetenskap

Organic bioelectronic devices to control cell signalling

AKADEMISK AVHANDLING
som för avläggande av medicine doktorsexamen vid Karolinska Institutet offentligen försvaras i Samuelssonsalen, Scheeles väg 2.

Tisdagen den 5 juni, 2012, kl 9.00

av

Karin Larsson

Huvudhandledare:
Professor Agneta Richter-Dahlfors
Karolinska Institutet
Swedish Medical Nanoscience Center
Institutionen för Neurovetenskap

Bihandledare:
Med Dr Gabriella Schmitz Lundkvist
Karolinska Institutet
Institutionen för Neurovetenskap

Fakultetsopponent:
Dr Keiichi Torimitsu
NTT Basic Research Laboratories
Atsugi, Japan

Betygsnämnd:
Docent Ulrica Edlund
Kungliga Tekniska Högskolan
Institutionen för fiber och polymerteknik
Avdelningen för polymerteknologi

Docent Anna Forsby
Stockholms Universitet
Institutionen för Neurokemi

Professor Mats Ulfendahl
Karolinska Institutet
Institutionen för Neurovetenskap

Stockholm 2012

ABSTRACT

The nervous system consists of a network of specialized cells that coordinate the actions of the body by transmitting information to and from the brain. The communication between the nerve cells is dependent on the interplay of both electrical and chemical signals. As our understanding of nerve cell signalling increases there is a growing need to develop techniques capable of interfacing with the nervous system. One of the major challenges is to translate between the signal carriers of the nervous system (ions and neurotransmitters) and those of conventional electronics (electrons). Organic conjugated polymers represent a unique class of materials that can utilize both electrons and ions as charge carriers. Taking advantage of this combined feature, we have established a novel communication interface between electronic components and biological systems. The organic bioelectronic devices presented in this thesis are based on the organic electronic ion pump (OEIP) made of the conducting organic polymer poly(3,4-ethylenedioxythiophene) doped with poly(styrenesulfonate) (PEDOT:PSS). When electronically addressed, electrochemical redox reactions in the polymer translate electronic signals into electrophoretic migration of ions. We show that the device can transport a range of substances involved in nerve cell signaling. These include positively charged ions, neurotransmitters and cholinergic substances. Since the devices are designed to be easily incorporated in conventional microscopy set-ups, we use Ca^{2+} imaging as readout to monitor cell responses. We demonstrate how electrophoretic delivery of ions and neurotransmitters with precise, spatiotemporal control can be used to modulate intracellular Ca^{2+} signaling in neuronal cells in the absence of convective disturbances. The electronic control of delivery enables strict control of dynamic parameters, such as amplitude and frequency of Ca^{2+} responses, and can be used to generate temporal patterns mimicking naturally occurring Ca^{2+} oscillations. To enable further control and fine-tuning of the ionic signals we developed the electrophoretic chemical transistor, an analogue of the traditional transistor used to amplify and/or switch electronic signals. We thereby take the first step towards integrated chemical circuits. Finally, we demonstrate the use of the OEIP in a new “machine-to-brain” interface. By encapsulating the OEIP we were able to use it *in vivo* to modulate brainstem responses in guinea pigs. This was the first successful realization of an organic bioelectronic device capable of modulating mammalian sensory function by precise delivery of neurotransmitters. Our findings highlight the potential of communication interfaces based on conjugated polymers in generating complex, high-resolution, signal patterns to control cell physiology. Such devices will have widespread applications across basic research as well as future applicability in medical devices in multiple therapeutic areas.

ISBN 978-91-7457-754-9