# - regulating cell signalling *in vivo* and *in vivo*, towards new therapy methods

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Abstract

Organic electronic materials are flexible, can conduct both electronic and ionic signal carriers, are bio-stable and -compatible, and can also be operated in hydrated environments. Together this suggests exploring devices and systems based on organic electronic materials to translate signals in between biological systems and electronics, to record and regulate process of eukaryotic cell systems. Here, an Organic Bioelectronics platform is reported, based on *iontronic* devices, in the form of resistors, diodes and transistors based on polyelectrolytes, which can process and dispense complex chemical patterns to regulate functions in cell systems, *in vitro* and *in vivo*. The Organic Bioelectronics platform has been explored in various applications, such as in cell biology and prosthesis applications.

# 1. Introduction

Conjugated polymers have been explored in electrochemical devices and systems, such as in sensors, electrochemical transistors and in electrochromic displays. Typically, these devices are built up from one or several device cells composed of two electrodes and a common electrolyte. As the two conjugated polymer electrodes are addressed with a potential difference electrochemistry will occur, i.e. one electrode will be reduced while the other one will be oxidized. Initially these two half-reactions also produces a potential gradient inside the electrolyte. If the resistive component of the electrolyte is relatively large, the electrochemical reaction is slow, thus the potential gradient inside the electrolyte is maintained over a long period of time. One popular conjugated polymer electrode system is the PEDOT:PSS material composition, where the PEDOT phase is the electronic conductor and the PSS phase serve as the polymeric counter ion, see Fig. 1.

In a neutral polymer electrolyte, both cations and anions can be conducted. The charge conductivity inside a polymer electolyte is for instance dependent on the morphology, dynamics of the polymer chains and also by the humidity. An example of a polymer electrolyte is PEG, see Fig. 1. The concentration, and also the transport, of ions inside polyelectrolytes are governed by the Donnan exclusion principle. So, a solid polyanion (polycation) film is a selective membrane for cations (anions). The polyelectrolytes can be considered as a p- and n-type charge transport system for ions. PSS and q-PVBC, see Fig. 1, are examples of a polyanion and a polycation, respectively.

In the Organic Bioelectronics platform, reported here, sets of two-electrode electrochemical cells based on PE-DOT:PSS are used to establish potential gradients and to convert electronic addressing signals into ionic ones. The PEDOT:PSS-electrolyte configurations are here connected to device configurations composed of combinations of films of polymer electrolytes and polyelectrolytes, defining the fundamental *iontronic* resistor, diode and transistor. Those devices, and circuits thereof, are then used to generate complex patterns of biological signals to regulate functions in biological systems.



Fig. 1 The materials used to construct the devices of the Organic Bioelectronics platform; PEDOT, PEG, PSS and q-PVBC, respectively.

# 2. The Iontronic resistor, diode and transistor

#### The iontronic resistor

The iontronic resistor is basically a linear strip of a polyelectrolyte conductor that selectively transport either cations or anions and that connects two PE-DOT:PSS-electrolyte configurations, see Fig. 2. As the electrodes are addressed, the ions of the source reservoir are transported to the target reservoir.

# The iontronic diode

The iontronic diode is built up from the combination of a polycation (eg q-PVBC) and a polyanion (eg PSS), placed in direct contact with each other, or separated by a neutral electrolyte (eg PEG). At forward bias, ions are accumulated along the bipolar membrane interface or inside the neutral electrolyte, thus enabling a large ionic current to pass through the device. At reverse bias, the interface or the neutral polyelectrolyte, is depleted from ions and thus the current is relatively much lower. The current rectification characteristics of such an ion biopolar membrane diode (IBMD) mimics the current rectification characteristics of the classical electronic pn-junction.

# The iontronic transistor

The npn-ion bipolar junction transistor (n-IBJT) is built up from the combination of a polycation emitter, a polycation collector, a neutral junction and a polyanion base (see Fig. 2). The collector, emitter and base are then all connected to a PEDOT:PSS-electrolyte configuration. As the base is positively biased, cations are injected into the polymer electrolyte junction. This forces the concentration of anions to also increase. The current through the junction is thus high and the transistor is now switched into the on-mode. If the cations are depleted from the base, also the concentration of anions turns low, thus the IBJT now operates in the off-mode. The ionic current-voltage characteristics of the IBJT are similar to the performance of an ordinary biplar junction transistor. Both npn- and pnp-version of the IBJT have been realized.



Fig. 2 The structure of the iontronic resistor (top), diode (IBMD, middle) and transistor (IBJT, bottom).

# 3. Iontronic circuits and applications

## Iontronic circuits

Various circuits composed of *iontronic* resistors, diodes and transistors have been realized, such as the full-wave four-diode ion current rectifier, smart pixels to achieve exclusive addressing in matrices, complementary inverters and NAND-gates, resistor networks. Some of these circuits have been applied in biological experiments to gain precise control over specific functions in cells, tissues and organs.

In one experiment an IBJT was utilized as the smart pixel to regulate the dispensing of a neurotransmitter to control the signalling in neuronal cells, *in vitro*. In a second experiment the iontronic resistor was positioned just outside the round window membrane of the cochlear of an animal model to regulate signalling *in vivo*.

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## Appendix

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