Combined EEG, pH and potassium solid-state ISE for migraine studies

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Migraine

- Characterized by severe headache and nausea
- Affects 12-28% of people at some point in life
- Start can be regarded as tipping point in the brain;
  - Activity in the brain spins out of control, causing a cortical spreading depression (CSD). It can be regarded as domino-effect.
Goal of the project

• Find markers for the onset of migraine attack
• How?
  o Leiden – Migraine specialists, discovers of a migraine gene
  o Provide the project with animal models with human migraine gene
  o Wageningen – analysis of data
  o BIOS: develop small measuring tools

• One of the tools to measure markers inside brain of mice that have the migraine gene:
  o Electrochemical probe
Electrochemical probe design

Specific recording sites for:
- Potassium
- pH
- EEG

100 µm
1.88 µm
Intermezzo: ion selective electrodes (ISE)

• Working principle of ISE:

Anion-selective solid-contact electrode

EC = electrode (electronic cond.)
CP = conducting polymer
ISM = ion-selective membrane
S = solution
e = electron
+ = ‘hole’ (oxidized CP)
L = ion-recognition site
○, □ = primary-, counterions

• ISM binds and transports specific ion from solution.
• Hence potential of ISM depends on concentration in solution (via Nernst).
• CP ‘acts’ as transducer between ions and electrons.
• EC senses chemical potential of ISM.
Conducting polymer deposition

- For conducting polymer it is important to NOT be pH sensitive

- PEDOT shows least pH dependence!
Conducting polymer deposition

- Oxygen concentration can also vary in brain

DC electrodeposited PEDOT

AC electrodeposited PEDOT

$O_2$ conc. is varied between 8 and 0.9mg/L
ISE characterization

- pH ISE
  - 3.5 % (wt) tridodecylamine + 2.1 % K-tetrakis, Dibutyl sebacate and 33.3 % Poly(vinyl chloride)

Calibration curve

$$y = -0.059 \times x + 0.71$$

Transient response
after pH step from 7.11 to 6.78

$$\text{Potential (V)}$$

$$\text{Time (seconds)}$$

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Transient behavior of EEG electrode

- It is important to have a fast response to be able to measure at high enough frequencies

Transient response of Platinum electrode after a pulse of 200kHz has been applied.
ISE characterization

- Potassium ISE
  - 2% valinomycin ionophore, 0.5 % Potassium tetrakis(4-chlorophenyl)borate for charge balancing, 65 % Bis(2-ethylhexyl)sebacate plasticizer and 32.5 % Poly(vinyl chloride)

- Linear response of 44mV/log(K⁺) in relevant range

- Na⁺ (cross) selectivity of -2.3
  \(10^{2.3} \approx 200\)
First measurements in model mice

- Potassium concentration during an induced CSD calculated from the measured potential

ISE electrode potential (blue) and calculated $K^+$ level (green). Black arrow indicates the start of the application of 1 M KCl on the dura overlaying the occipital cortex for the local induction of SD. KCl was present throughout the recording session.

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