Supplementary Information S1

Quantitative Analysis of a pH-Sensitive EISCAP Urea Biosensor Using a Simplified Kinetic Model: Parameter Estimation and Matrix Effects

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Poster S1

Detection of urea in artificial urine using capacitive field-effect biosensors modified with a stacked polyelectrolyte-enzyme bilayer

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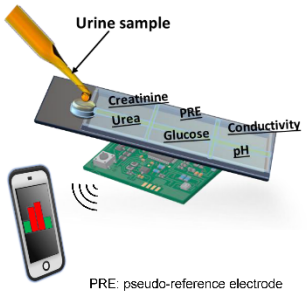
Introduction

Urinary biomarkers are important parameters for monitoring medical conditions related to kidney disfunctions, urinary tract infection and diabetes.

A concept for an array of digital biosensors (UroLogicChip) based on electrolyte-insulator-semiconductor capacitors (EISCAP) for the point-of-care (especially, at homecare) testing of clinically relevant urinary biomarkers (urea, creatinine, glucose) is presented. The UroLogicChip will be able to provide measurement results in a YES/NO format, allowing the rapid and reliable assessment of the overal physiological condition.

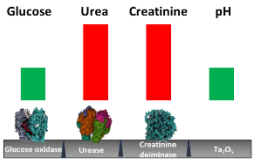
Experimental results for the detection of urinary biomarker urea in phosphate buffer and artificial urine using EISCAPs modified with a stacked polyelectrolyte/enzyme urease bilayer are presented. A theoretical kinetic model of the urea-sensitive EISCAP biosensor was developed and compared with the experimentally observed results.

UroLogicChip concept

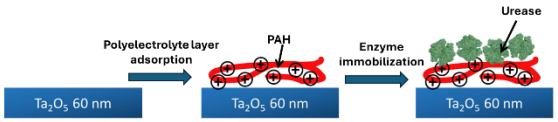


PRE: pseudo-reference electrode

- Digital display of the results in YES/NO format with cut off values for each biomarker
- Easy-to use
- Homecare, in-field settings
- Non-invasive method
- Exchangeable and combinable

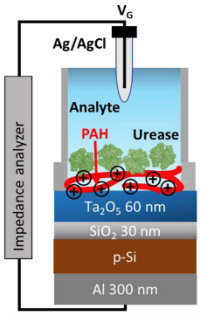


EISCAP surface modification

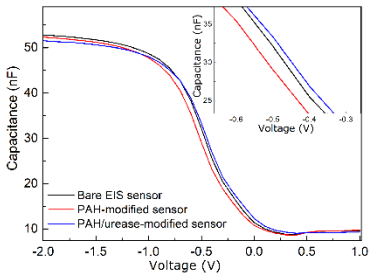


PAH: poly(allylamine) hydrochloride

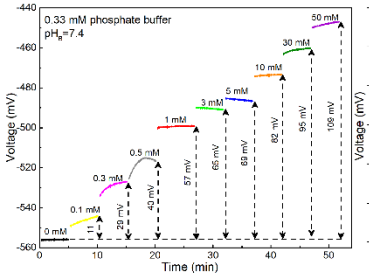
Urea-sensitive EISCAP biosensor



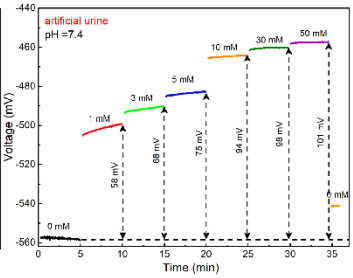
Capacitance-voltage curves



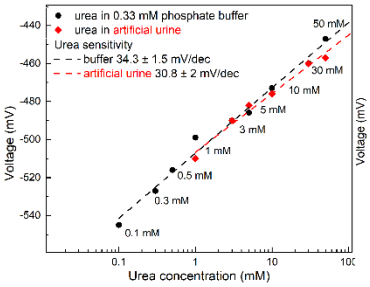
ConCap response of urea-sensitive EISCAP in buffer



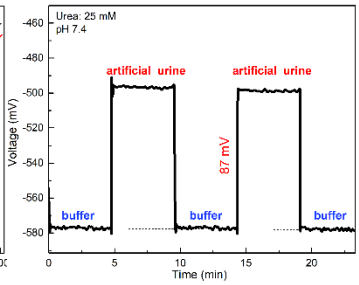
ConCap response of urea-sensitive EISCAP in artificial urine



Calibration curves



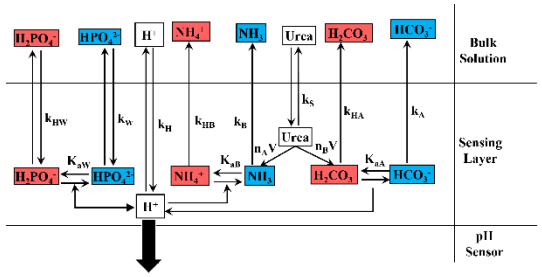
Reproducibility



Urea/urease enzymatic reaction

$$NH_2-CO-NH_2(\text{urea}) + 3H_2O \xrightarrow{\text{urease}} CO_2 + 2NH_4^+ + 2OH^-$$

Kinetic model of urea-sensitive EISCAP by Glab et al. [1]



The key aspects of the kinetic model are listed below:

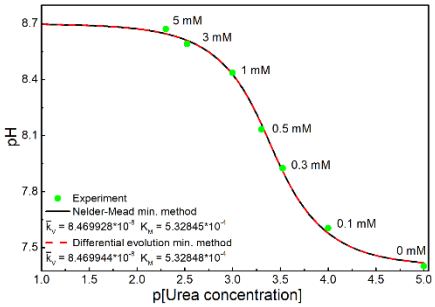
1. The geometry of the enzyme layer does not have to be defined in kinetic model.
2. Enzymatic reaction takes place by Michaelis-Menten kinetics, where the hydrolysis reaction rate is determined as:

$$V = \frac{V_{max}[S]}{K_m + [S]}$$

where **V** and **[S]** denote the actual rate and concentration of the substrate in the enzymic layer, K_m, is the Michaelis-Menten constant and V_{max} the maximum reaction rate.

3. All the species except for the enzyme can diffuse through in both directions of the enzyme layer, with transport rates proportional to the concentrations of the species.
4. The buffering components as well as the protolytic acid and base products of the enzymatic reaction are in protolytic equilibria, and the dissociation constants are the same as in the buffer solution.

Fitting of the experimental results to the kinetic model



The comparison of the experimental data to this model allows to determine the relevant enzyme kinetic parameters: reaction rate (V_{MAX}) and Michaelis-Menten constant (K_m), which are of importance in the design and optimization of sensor parameters.

$\overline{k_s}$ - normalized reaction rate (V_{MAX}/k_s)

Conclusion

The obtained results demonstrate the suitability of PAH/urease bilayer-modified EISCAPs for the urea detection in artificial urine samples with a sensitivity of 30.8 mV/dec and good reproducibility.

References

[1] Glab, S.; Koncki, R.; Hulanicki, A. Analyst, 116, 453 (1991).

Acknowledgements

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