

## **1 Abstract**

- overview over conventional biosensors
- possibilities, challenges of the new idea
- how the idea works

## **2 multiple biochemical coupling of signal processing with chemical actuators**

- prospects
- fundamental and practical challenges
  - attention to composition, preparation and immobilization of the bio-computing surface layer
  - success depends in part on immobilization of the biocomputing reagent layer
  - system scalability
  - efficient transduction of the output signals
- high fidelity

## **3 common biosensing devices**

- based on single input (analyte)

## **4 Layers**

## **5 begriffe**

unconventional computing = quelle

## 6 Chemical computing

- processing information by chemical means
- single logic gates (mimicking Boolean) to small logic networks

## 7 biocomputing

- biomolecular systems for processing chemical information
- more complex than nonbiological systems

## 8 overview of the evolution of biomolecular systems

- general concept
- multisignal digital biosensors processing complex pattern of different physiological markers
- practical considerations
- challenges

### 8.1 motivation

- common biosensing devices
  - single input
- multisignal logic gates /biochemical logic systems /biocomputing sensor systems

Beschreibung

- multiple target analytes(inputs) (enzymegates)/biochemical inputs
- high-fidelity biosensing compared
- rapid and reliable assessment of physiological condition (enzymes + automatically processing)
- optimal timely therapeutic intervention

- overview of the novel research paradigm of digitally operating biosensors logically processing multiple biochemical signals through Boolean logic networks composed of biomolecular systems
- realization of closed-loop systems (sense/act/treat)

## Chancen

- biomedical monitoring (example, closed-loop- $\hat{c}$  patient tailored timely therapy, personalized medicine = sensing devices + delivery devices)
  - \* closed-loop - $\hat{c}$  patient tailored timely therapy possible
  - \* sensing devices + delivery devices = personalized medicine
  - \* example feedback-loop: diabetes: electrochemical glucose sensing element + insulin-delivery feedback loop
  - \* fast delivery in emergencies
- environmental monitoring
- national defense
- food safety

## 8.2 enzyme logic gates

- coupling enzymatic reactions (logic gates) with electronic transducers and signal-responing materials

- examples

1

- glucose oxidase and catalyse operating as logic gates:
- input :  $H_2O_2$  and glucose
- gluconic acid = biocatalytic oxidation of glucose
- only when both present optical output signal. = AND
- define logic values: small changes = 0 and large absorbance changes as 1 =  $\hat{c}$  AND
- similar possible with XOR, AND, OR, NOR, INHIBIT

- with logic gates with modular structure that enables their assembly in networks NAND/ NOR possible

2

- pH changes in solution as logic responds to input signals
- AND invertase + glucose oxidase (from 5.8 to 3.5)
- OR esterase and glucose oxidase in glucose and ethyl butyrate - when one of both present - acidification
- neutral pH = 3.5

Conclusion:

- don't solve real computing problem nor operate as useful biosensors
- represent first step toward the development of digital biosensors
- funfact optimization of enzymatic reaction, up to 10 logic gates concatenated with low noise in the system

### 8.3 Enzyme logic circuits-scaling up the system complexity

- main challenge: scaling up the complexity of the systems by networking the individual parts of a logic circuit
- addressed experimentally when designing networks composed of concatenated enzyme logic gates
- assembled logic networks analyzed theoretically for optimization and noise reduction; coupling output signals with electronic transducers and bio-electronic devices

### 8.4 Biomolecular logic gates designed for biomedical analytical applications

- logic gates and their networks = biomolecular information processing systems
- = biosensoric systems with logically processed signals represented by various biomarkers (characteristic of different abnormal physiological conditions)

- problems not addressed yet:
  - logic 0 values were defined as the absense of the enzymes
  - logic 1 not always correspond to the concentration expected in vivo /not normal physiological concentrations
  - input not justifies to their biomedical meaning

## 8.5 ENzyme logic system recognizing various injury-related physiological conditions

- types of injuries result in concentrations of chemical substances in the body
- example: lactate axidase, horeserasish peroxidase and glucose dehydrogenase = designed to process biochemical information related to pathophysiological conditions from brain injury
- markers: glucose(hemorrhagic shock),lactate(rhagic shock or traumatic brain injury) and norepinephrine(tramatic injury)
- logic 0 = normal concentrations
- change results into different numbers 1,2,3 - convenient
- = biocomputing logic system
- challenge: difference between normal and unnormal minimal = $\epsilon$  not linear, should be sigmoidal

## 8.6 hardware

## 9 Aufbau

- Abstract: Biosensoren, logic gates, possibilities, challenges and future work
- introduction Definition, possible fields(examples), special,... loops
- The idea Theory and practical
- Two examples

- Layers, challenges and future work
- conclusion