Multisignal digital biosensors- digital Biosensors integrated with enzyme logic systems

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Abstract. While common Biosensors,analytic devices to convert a biological response into a electrical signal, are based on single input, this report concentrates solely on biosensors processing multiple biochemical signals.

- biochemical logic systems
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Keywords: Biomolecular computing · Biosensors · enzyme logic gates · biosensing · biocomputing systems · enzyme logic circuits · biomedical applications

1 Introduction

- common biosensing devises are based on a single input
- high-fidelity compared
- closed loop/feedback loops possible (sense/act/treat)
- rapid and reliable assessment of overall physiological condition
- could initiate optimal timely therapeutic intervention
- application og biomolecular logic systems for analystic purposes could yield a novel class of biosensors: many input signals and binary outputs
- logically processed feedback between drug appl. and physiological conditions can signifacntly imprive drug targeting and efficiency

- Biosensors + enzymes

2 motivation

- high-fidelity
- rapid and reliable assessment of overall physiological condition
- optimal timely therapuetic intervention
- feedback-loops
- biomedical monitoring(example, closed-loop-¿ patient tailored timely therapy, personalized medicine= sensing devices + delivery devices)
  - closed-loop -¿ 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

3 concept

3.1 Biosensors: layers

A Biosensor is a device that transforms biochemical information, into an analytically useful signal. It contains usually the two basic components, the receptor

- immobilization of the biocomputing reagent layer
- transducer layer
- parallel or single

3.2 Biocomputing: concept

allgemein assembling of single logic gates in concentrated logic cascades and complex branching networks is a chemical analogue to designing of computer hardware. analysis of the chemical output signals generated by biomolecular logic systems is often limited. to digitalize chemical process two levels of concentrations of chemical reaction species are considers as input signals. 0 = usually absense of enzyme. 1 significantly different to absence. the chemical inputs are applied in different binary combinations (Katz)

- biomolecular logic systems: definiton
- subarea of chemical computing
- single logic gates to small logic networks (for example half-adder/ half subtractor)
- biomolecular systems for processing chemical information
- different biomolecular tools (including proteins/enzymes) assemble biocomputing systems processing biochemical information

what would bring it to biosensors

- Enzyme logic system: multiassemblies to perform simple arithmetic functions
- idea: applicatoin of biomolecular logic system for analytical purpose new class of biosensors that accept many input signals and produce binary outputs in form yes/no
- example analyse protein libraties associated with muliple sclerosis(58)

how enzme-based logic gates work Enzyme logic gates

- enzymatic reactions
- coupling of logic gates with electronic transducers and signal responsive materials
- transducers:
- signal responive material

example theoretical with graphics

- glucose oxidase and catalyse operating as logic gates:
- input : H2O2 and glucose
- gluconic acid = biocalatyltic oxidation of glucose
- only when both present opical output signal. = AND
- define logic values: small changes = 0 and large absorbance changes as 1 =¿ AND
- similar possible with XOR,AND, OR, NOR, INHIBIT
- with logic gates with modular structur that enables therir assembly in networks NAND/ NOR possible
- 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)

example ph

- pH changes in solution as logic respones to input signals
- AND invertase + glucose oxidase (from 5.8 to 3.5)
- OR ersterase 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

for biochemical analytic applications

- design of biosensoric systems with logically processes signals represented by varous biomarkers characteristic for different abnormal physiological conditions

3.3 Biosensors logic systems

Biosensors logically processing multiple biochemical signals
-such procassed information produces a final output yes/no
- boolean logic networks composed of biomolecular systems

- multiple target analytes(inputs) for enzyme gates
- high-fidelity compared
- closed loop/feedback loops possible (sense/act/treat)
- rapid and reliable assessment of overall physiological condition
- could initiate optimal timely therapeutic intervention
- biosensors + enzyme logic gates
- allows direct coupling of signal processing with chemical actuators
- application og biomolecular logic systems for analystic purposes could yield a novel class of biosensors: many input signals and binary outputs
- logically processed feedback between drug appl. and physiological conditions can signifacntly imprive drug targeting and efficiency
- difficulties: complexity by assembling individual logic gates into complex logic networks (intelligent by molecular logic) (43-34-67)
- new approach for the sensor design and operation, interfach biocomputing system and electronic transducers

4 possible application

- not just chronic but also ....
- state of the art
- feedback loop currently devoted to management of diabetes through integration of an electrochemical glucose sensing element with an insulin-delivery feedback loop for the optimal dose of insulin (69-71)
- example analyse protein libraties associated with muliple sclerosis(58) 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 traumic brain injury) and norepinephrine(traumatic injury)
  - logic 0 = normal concentrations
  - change results into different numbers 1,2,3 - convenient
  - = biocomputing logic system
  - challenge: difference between normal and unnormal minimal =¿ not linear, should be sigmoidal

5 considerations

stabilization and confinement// optical transduction

5.1 surface immobilization of the biocomputing machinery

- optimal surface confinement of the biocomputing layer
- engineering enzyme microenvironment (transducer layer)
- contact between biocomputing layer and transducing surface
- combine individual logic-gates and maintain high enzymatic stability and reataining individual reagents
- leakage of cosubstrate
- no cross-reactions
- surface confinement? layer-by layer? more efficient and rational
- level of the surface confined reagents tailored for account of different input concentrations /enzyme activities
- coating: optimized for transport and excluding potential interfernece and protecting the surface

5.2 optimal transduction of biocomputing signal processes

- simultaneous measurements of multiple outputs require different transduction strategies (common: fixed potential)

- Requires:interface of biocomputing systems + electronic transducer
  Therefore
- scalability (increasing nuber of logic gates, assembling into complex networks)
- complexity(coupling of gates abd non boolean elements)
- composition, preparation and immobilization of the biocomputing surface layer
- layer by layer
- optimal surface confinement
- careful engineering of the enzyme microenvironment(on transducer surface) for performance
- biocomputing layer + transducing layer + combine individual logic-gate elements

6 Conclusion

good but needs lot of work
sums up bla

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