MOLECULAR BIOSENSOR FOR DETECTING METALS: USE OF COMPUTATIONAL MODELING

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• METAL IONS ARE MIXED IN NATURE BECAUSE OF THE CHEMICAL CONFIGURATION.

• THE NEGATIVELY CHARGED CELL WALL IS GOING TO INTERACT WITH METAL IONS.
• CATION PORPHYRINS ARE FOUND IN NATURE, THUS THEY CAN BE USED AS MARKER FOR CONTAMINATION.

• CATION PORPHYRINS, Zn, Cu, Fe ENHANCE RNA EXPRESSION IN FUNGI (CUERO et al 2003) THEREFORE, THEY CAN BE USED AS MARKER AND BIOSENSORS. HOWEVER, MOST BIOSENSORS ARE ONLY CAPABLE TO DETECT SINGLE IONS
Metals Bound to the Negative Charged Sugar-Phosphate of DNA

Figure 1
• APPROACH:

• PLASMID ISOLATION AND SYNTHESIS OF NEW GENES SEQUENCES.
• NEW PARTS.
• PREPARATION OF COMPETENT CELLS
• CELL TRANSFORMATION
• TEST IN DIFFERENT ENVIRONMENTAL CONDITIONS (CONCENTRATIONS OF METALS, O2, PH, CO2)
PARTS AND CHASSIS

- pUC57
- E. COLI
- M. LUTEUS
- ION CHANNELS
- RIBOSOMAL BINDING SITES
- ANIONIC AND CATIONIC METALS
- CYTOCHROME C
<table>
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Figure 4
Constructed PV-Trimetallic-gene probe: pUC57-S-3M
Figure 5. Growth of the pUC57-S-3M Transformed Micrococcus luteus Cells in Comparison with Non-transformed M. luteus (ATCC #4698)

A. Non-transformed cells
B. Transformed cells
PARAMETERS

- CFU
- DNA CONCENTRATION
- DNA FL
- PROTEIN FL
- ATP
- CYTOCHROME C

*COMPUTATIONAL MODELING.*
Ion Channels

- Proteins
- Allow the movement of ions across cell membrane
- Extremely specific gateways
Ion Channel and Electron Transport Connection
Ion Channel and Electron Transport Connection

• High recognition for transport of iron
  – Can specify other ions (vanadium, nickel, etc.)
• Ions release protons (H\(^+\)) into cell and deposit electrons inside plasma membrane
• Receptors embedded in membrane receive electrons
Cytochrome C and Molecular Biosensor

- Cytochrome C
  - its role in the E.T.C-carrying electrons-produces ATP-more DNA-more cell replication
  - overall enhancing our biosensor

- Help produce a sensor that can detect metals in low concentrations.
ATP in DNA

Cuero Lab
Genetic machine
Promoter (P1/P2 alone)

Control

Biobrick without ion channel

0 hours

18 hours

DNA: 3.7 ng/ul  ATP: 675 fsu
BACTERIAL GROWTH (O.D.) = 0.1

DNA: 8.8 ng/ul  ATP: 1288 fsu
BACTERIAL GROWTH (O.D.) = 2

0 pmm
Computational-Modeling Synthetic Biology
Artificial Neural Network Modeling of A Molecular Biosensor

• Neural Networks
• Use of the artificial neural network
• Preliminary training of the network
• Results
• Principle units of metal biosensor
• Future work
• electronic Nose (eNose)
• Application of the eNose to the molecular sensing device
Artificial Neural Network Modeling of A Molecular Biosensor

From the biggest brain…….

To the smallest brain…..
Artificial Neural Network Modeling of the Molecular Biosensor
Representation of a layer of a neural network

\[ \sum \]

\[ z = \sigma(\beta) \]

\[ \beta = \sum_{i=0}^{n} w_i x_i \]
Preliminary Network
Training by fitting to a function

- Training using back propagation
  - Select function in matlab library to fit data
  - Find error, and compare to target error
  - General error function: \( E = \frac{1}{2} \sum_{o=1}^{N_o} (\delta_o - y_o)^2 \)
  - Finally select function that gives least error
  - Sigmoid function: \( \sigma = \frac{1}{1 + e^{-x}} \)
Validation of network performance

- Select representative data from data used in training step
- Input selected data into the network and compare closeness of fit
- Closeness determines the correctness of the transfer function eg.
Testing performance

- Select data that was not used in testing and validation datasets
- Compare network output to actual value from experimental data
Matlab representation
Results (Cont’d)

• Performance of network
Emergent Representation
## Results

- Example of data for training, validation, and testing the neural network

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Principle units of the metal Biosensor

Ion(s) in solution → Biosensor → Neural Network → Fluorescence
Principle units of the metal Biosensor

Ion(s) in solution → Biosensor → Neural Network → Fluorescence
Comparison (Theoretical vs Actual)
What is the eNose?

An eNose is an analytic device originally used for detecting chemicals and their concentrations in vapors.

How can this be applied to the metal ion sensor?

By finding the functional relationship, which is the response to the concentration and type of metal.
The fundamental eNose algorithm relies on the equations:

\[ r_{ij} = f_{ij}(c_j) \]

\[ c_{j} = \frac{1}{m}(c_{ij} + c_{2j} + \ldots + c_{mj}) \]

\[ \sigma_{j} = \frac{1}{m-1} \left[ (c_{1j} - \bar{c}_j)^2 + (c_{2j} - \bar{c}_j)^2 + \ldots + (c_{mj} - \bar{c}_j)^2 \right]^{-1} \]

where

\[ r_{i} = f_{ij}(c_{ij}) \]

\[ r_{i} = \text{response of species } i \text{ as a function of concentration} \]

\[ c_{ij} = \text{concentration of species } i \text{ in } j^{th} \text{ sensor} \]
Future Work

• Experimental data for individual metal ion protein sequence, and ligations

• Wider range of variation in the concentrations

• Data from rejected samples to determine the reliability of network

• The completion of the final network to identify the ion as well as it’s corresponding concentration
Principle units of the metal Biosensor

Ions in solution → Biosensor → Neural Network

Metal Ion
Concentration
Prairie View A&M
Cuero Lab