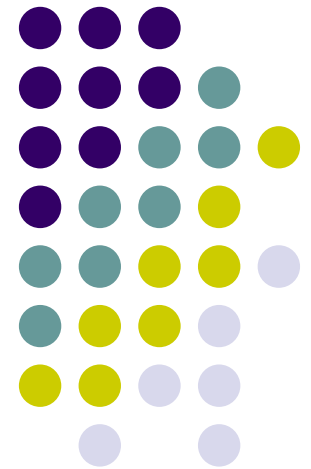


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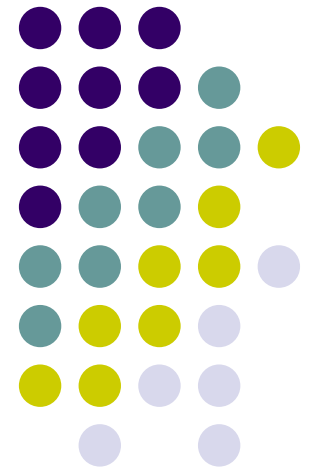
By: Lim Ai Tee

Supervisor: Dr Lee Chew Tin

Modeling of Insulin Binding System Using Artificial Neural Network



INTRODUCTION





Diabetes mellitus

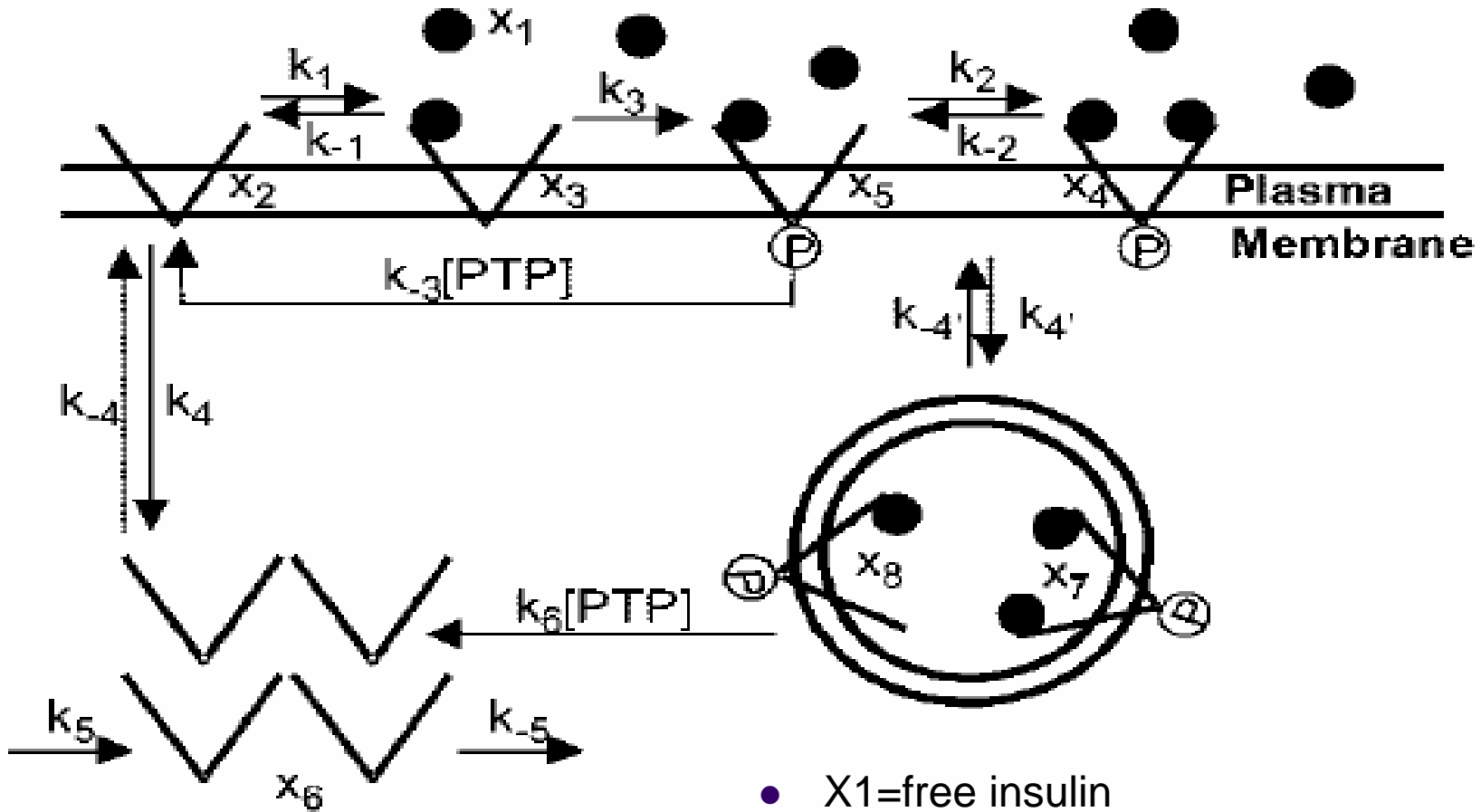
the world's most common metabolic disorder

- Estimated over 175 million person worldwide are afflicted with the diabetes in year 2000
(International Diabetes Institute, WHO)

Heterogeneous disorder
Factor: environmental and genetic

**Insulin signaling pathway plays a
pivotal role in this disease**

INSULIN BINDING SYSTEM



- X_1 =free insulin
- X_2 =free receptor
- X_3 =1 insulin + receptor
- X_4 =2 insulin + receptor + phosphorylated
- X_5 =1 insulin + receptor + phosphorylated

Problem Statement:



- Insulin receptor binding are complicated
- It is believe that failure binding will contribute to **Diabetes type II**
- These binding mechanism are still not well characterized



Objective:

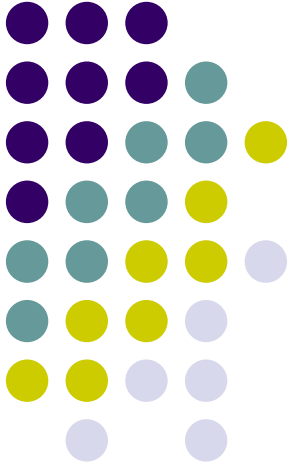
- To build a metabolite **correlation model** for Insulin Binding Pathway using Artificial Neural Network

Scope:

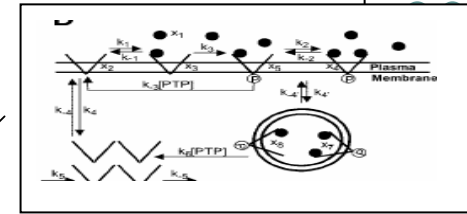
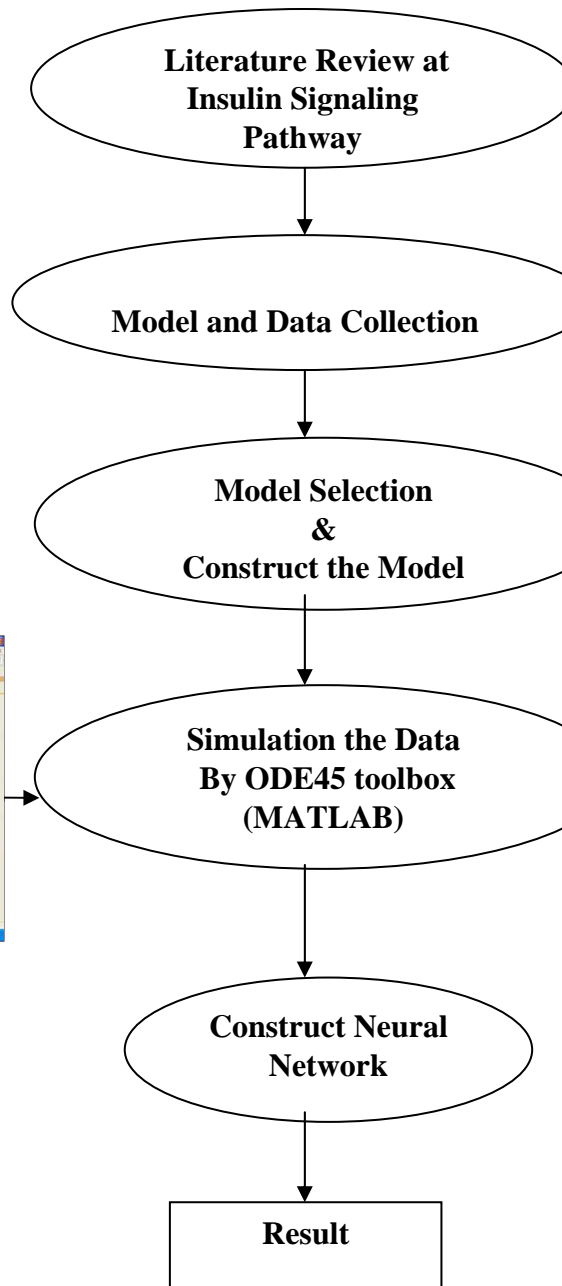


- **Simulate the time course** for output metabolites in Insulin Binding System using **ode45 toolbox** (MATLAB)
- **Construct and validate** Insulin Binding System **model** using **Artificial Neural Network** (MATLAB)

METHODOLOGY

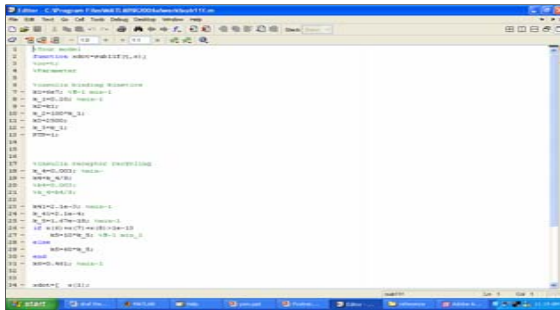


Methodology:

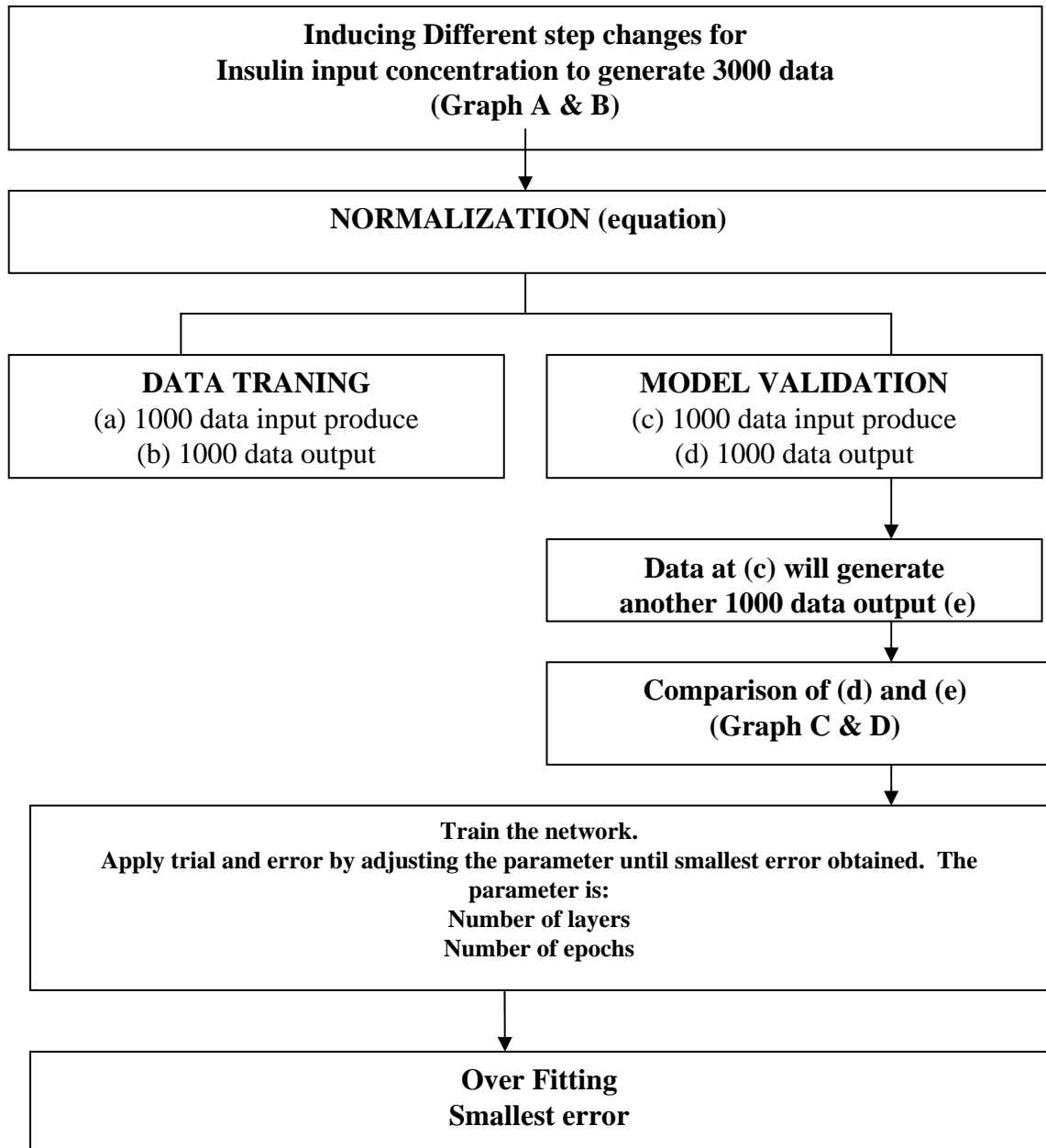


$$\begin{aligned}
 x_1 &= \text{insulin input} & (6) \\
 dx/dt &= k_{-1}x_0 + k_{-2}[PTP]x_5 - k_{1x}x_2 + k_{-4}x_6 - k_4x_2 & (7) \\
 dx/dt &= k_{1x}x_2 - k_{-1}x_3 - k_3x_3 & (8) \\
 dx/dt &= k_2x_3 - k_{-2}x_4 + k_{-4}x_7 - k_4x_4 & (9) \\
 dx/dt &= k_3x_3 + k_{-2}x_4 - k_3x_3x_5 - k_{-3}[PTP]x_5 & (10) \\
 & \quad + k_{-4}x_6 - k_4x_6 & (10) \\
 dx/dt &= k_5 - k_{-5}x_6 + k_6[PTP](x_7 + x_8) + k_4x_2 - k_{-4}x_6 & (11) \\
 dx/dt &= k_4x_4 - k_{-4}x_7 - k_6[PTP]x_7 & (12) \\
 dx/dt &= k_4x_5 - k_{-4}x_8 - k_6[PTP]x_8 & (13)
 \end{aligned}$$

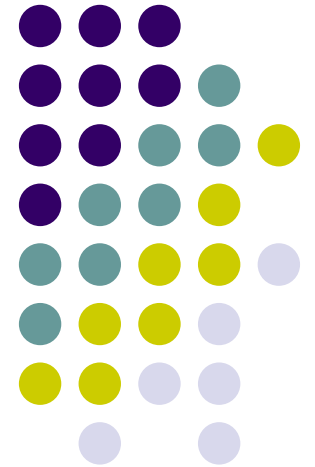
$$\begin{aligned}
 k_1 &= 6 \times 10^7 \text{ M}^{-1} \cdot \text{min}^{-1} \\
 k_{-1} &= 0.20 \text{ min}^{-1} \\
 k_2 &= k_1 \\
 k_{-2} &= 100k_{-1} \\
 k_3 &= 2,500 \text{ min}^{-1} \\
 k_{-3} &= k_{-1} \\
 k_4 &= k_{-4}/9 \\
 k_{-4} &= 0.003 \text{ min}^{-1} \\
 k_4 &= 2.1 \times 10^{-3} \cdot \text{min}^{-1}
 \end{aligned}$$



Construction neural network:

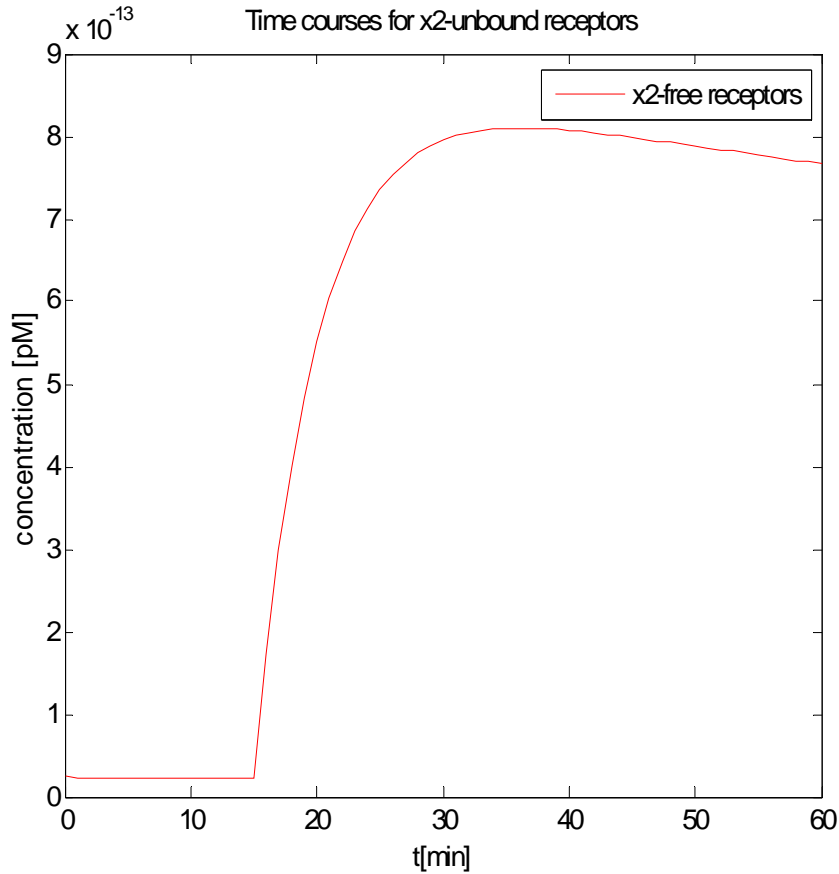


RESULT & DISCUSSION



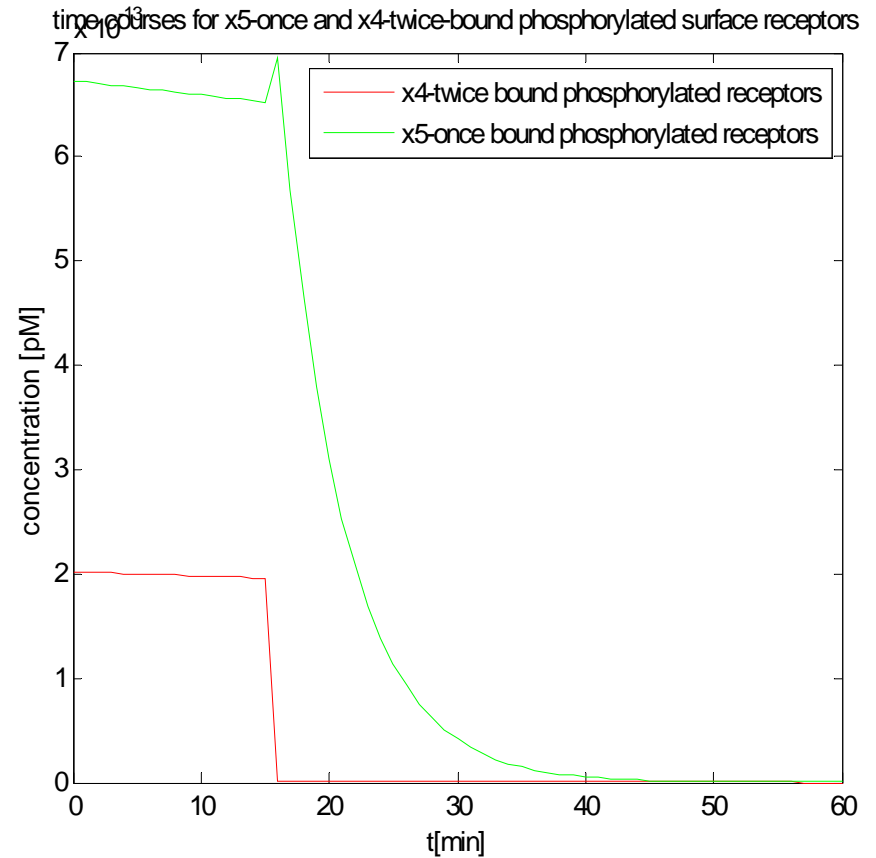
Graph insulin binding system:

A



A- Time courses for unbound receptors(x2)

B

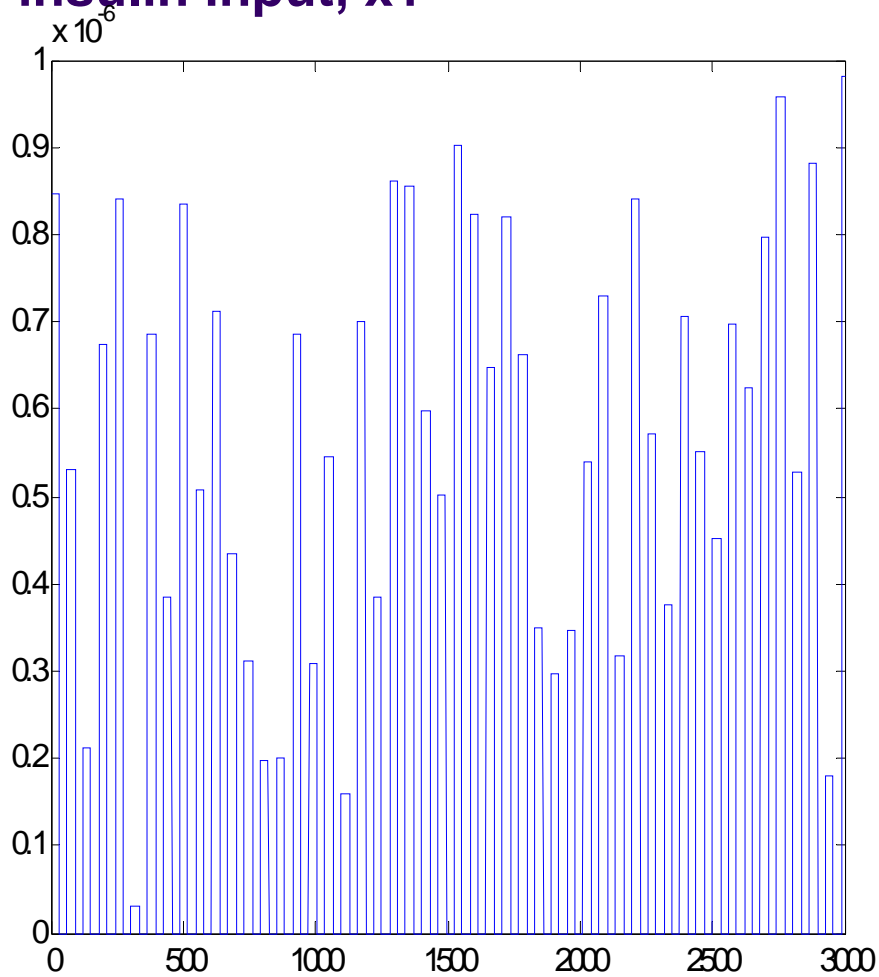
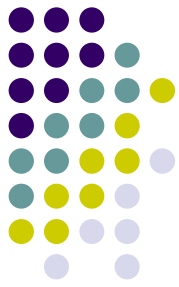


B-Time courses for once(x5)-twice(x4) phosphorylated receptors

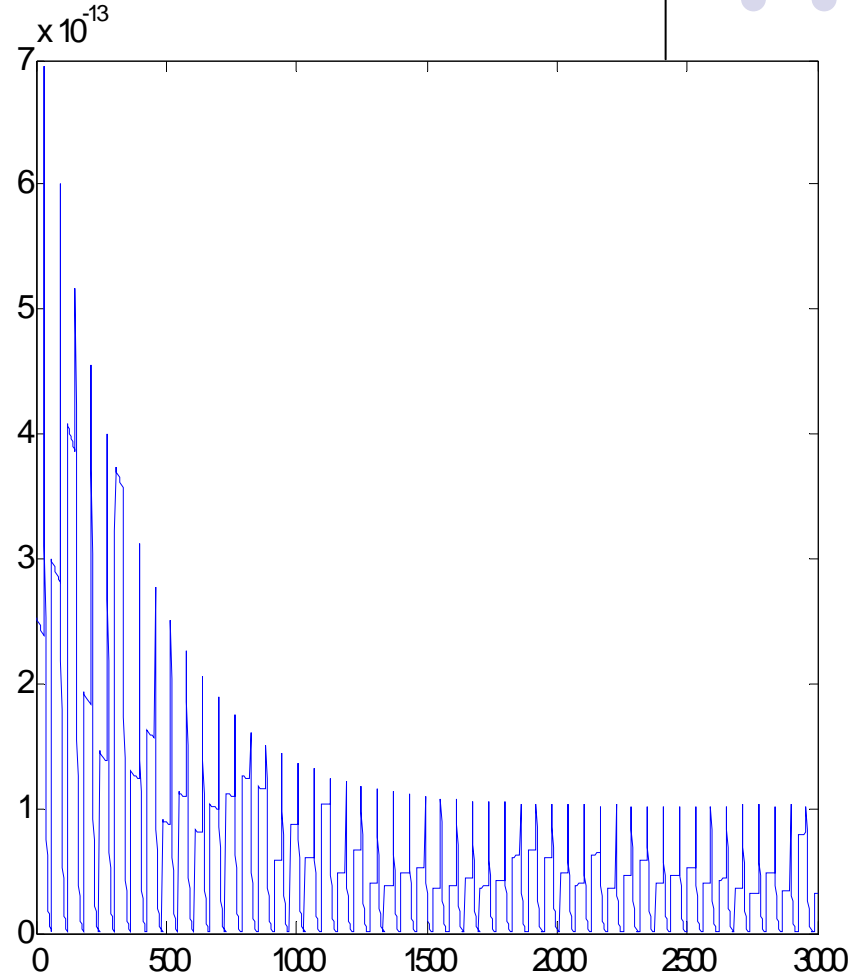
Training data set:

A: Step changes of insulin input, x1

B: Dynamic response of x5 for different step change of insulin input, x1



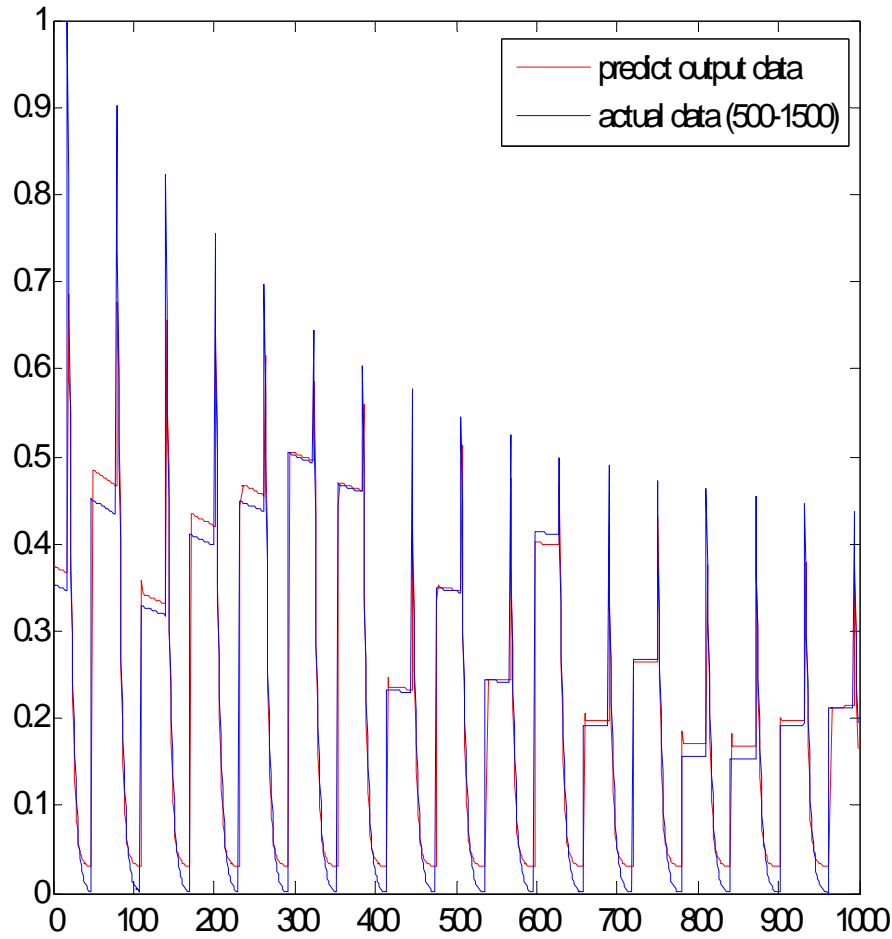
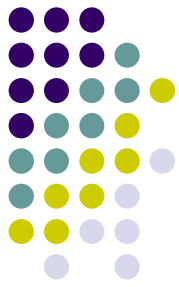
A (input=insulin)



B (output= x_5 [IRP])

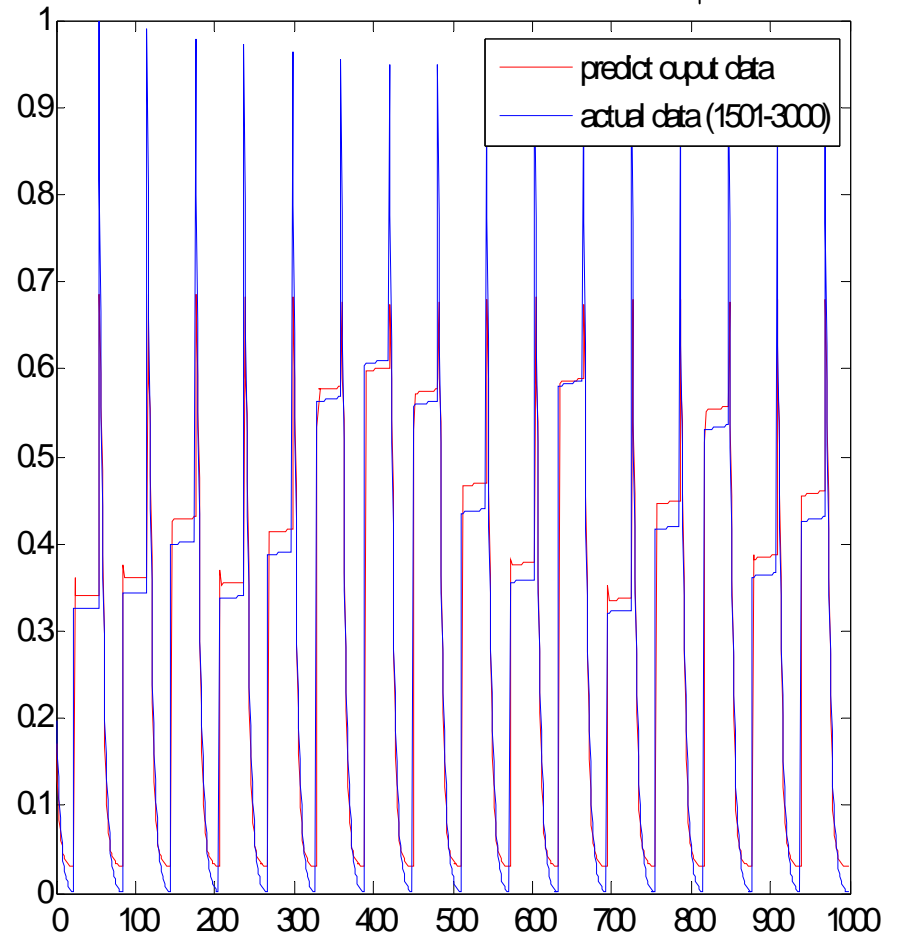
Validation data:

C & D: Normalization → Generalization output



C

TRAINCGB: Epoch 59/300, MSE 0.00361091



D

Conclusion:



- A range of time course output concentration of metabolites
 - x2-free receptor
 - x4-phosphorylated twice-bound receptors
 - x5-phosphorylated once-bound receptorsfor insulin binding system has been simulated using the ode45 toolbox.
- A correlation model for predicting the output concentration of metabolites for insulin binding system is successfully developed using Artificial Neural Network.

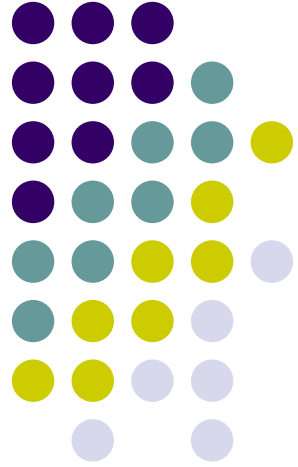
Acknowledgment:



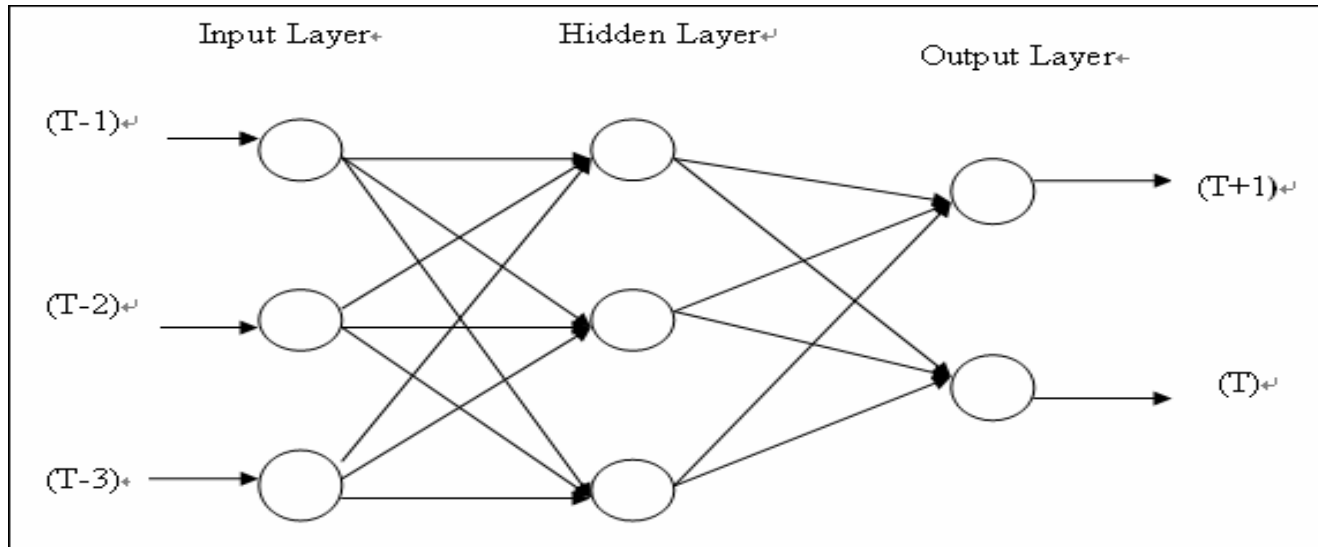
Thanks you to:

- Dr. Lee Chew Tin
- Mr. Shia Yik Ling
- Ms. Chew Yin Hoon
- Metabolic team members

THANKS YOU !!



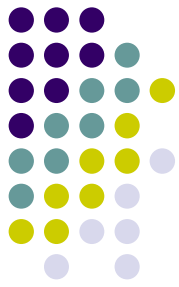
Artificial Neural Network:



- Best alternative for output estimation
- ability to learn and generalize from experience and to adapt to changing situation
- Network used- feed forward back propagation
- Algorithm-traincgb

Continues,

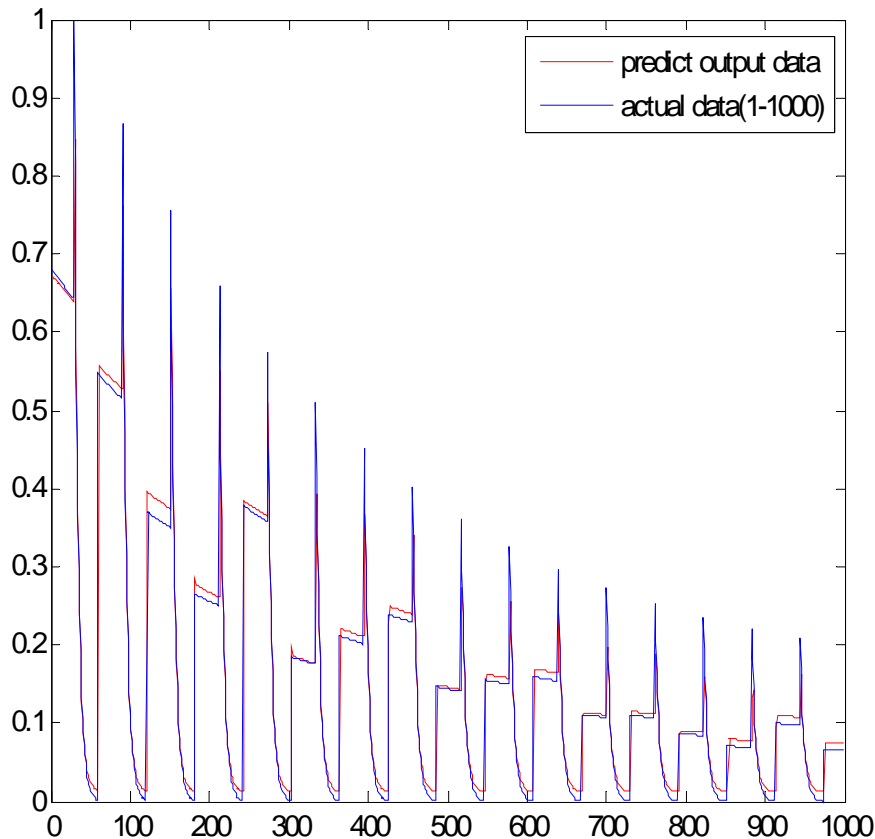
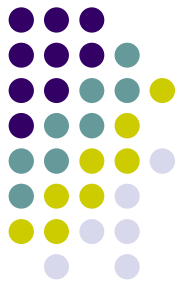
- Transfer function (TF)
 - transfer the output of an network layer
 - using—tansig (hyperbolic tangent sigmoid TF)
 - purelin (linear TF)
- Training function
 - train network
 - using ---traincgb (Powell-Beak conjugate gradient back propagation TF)
- Learning function
 - learning algorithms used to adapt networks
 - using---learngd (gradient decent weight)
- Performance function
 - MSE (mean square error PF)



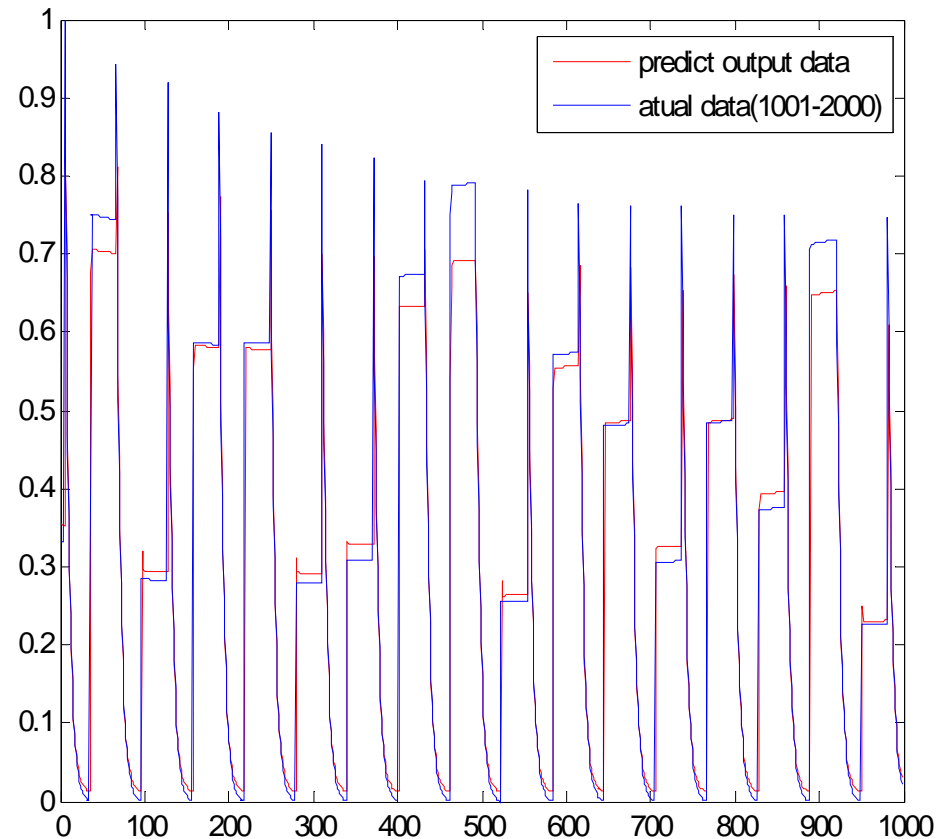
Validation data set:

C: Step change of insulin input(x1) for Generalization

D: Dynamic response of x5 for different steps change of insulin input (x1)



C



D

TRAINCGB, Epoch 224/300, MSE 0.0024066/1e-005