

# Enzyme Computing

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# DNA Computing

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- Parallel computing
- Faster and smaller
- There are problems with scaling
- DNAzyme, Enzyme, toehold exchange,  
Algorithmic self-assembly

# Enzyme Computing

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- Itamar Willner, 2006
- Insert into body
- Compute **metabolic pathway**
- Drug delivery
- Monitor the growth of cells

# Logic Gates

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- ◉ Type : AND 、 OR 、 XOR 、 InhibA
- ◉ Input : GOx 、 GDH 、 AlcDH 、 MP-11
- ◉ Output : spectral changes

# Input Enzymes

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- ◉ GOx : glucose oxidase
- ◉ GDH : glucose dehydrogenase
- ◉ AlcDH : alcohol dehydrogenase
- ◉ MP-11 : microperoxidase-11

# Output : Spectral Changes

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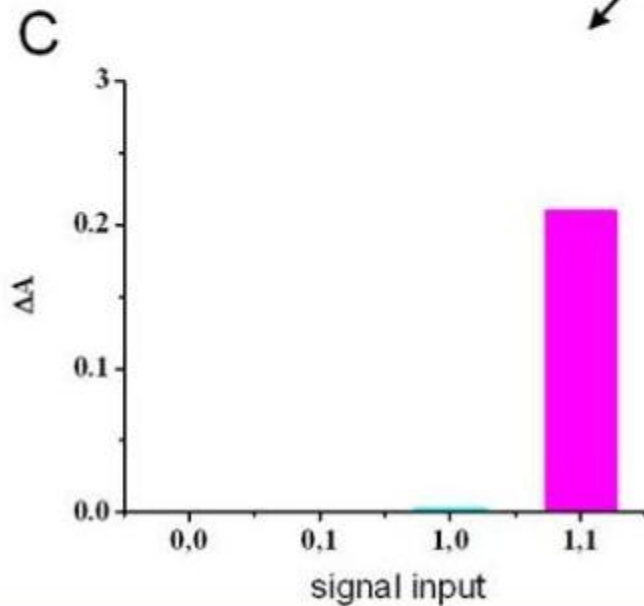
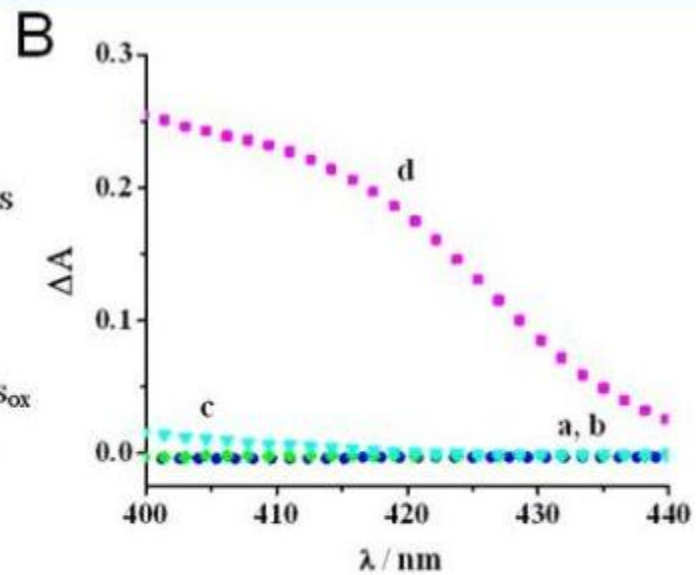
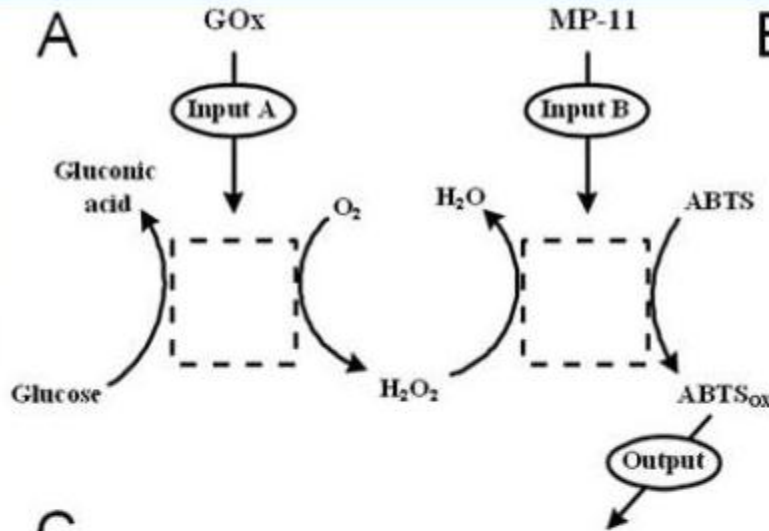
- ◉ **ABTS** : absorb  $\lambda = 420 \text{ nm}$
- ◉ **NADH** : absorb  $\lambda = 260 \text{ nm}$  &  $340 \text{ nm}$
- ◉ **NAD<sup>+</sup>** : absorb only  $\lambda = 260 \text{ nm}$

# AND Gate

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- ⦿ Solution containing **glucose, oxygen, and ABTS.**
- ⦿ Absorbance  $\lambda = 400 \sim 440 \text{ nm}$
- ⦿ Note that H<sub>2</sub>O<sub>2</sub> does not exist in original composition of the gate

# AND Gate



**D**

Input A GOx	Input B MP-11	Output AND
0	0	0
0	1	0
1	0	0
1	1	1

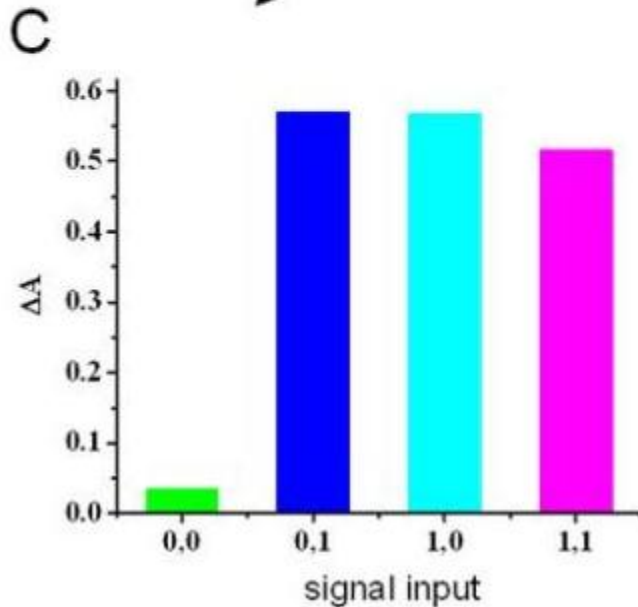
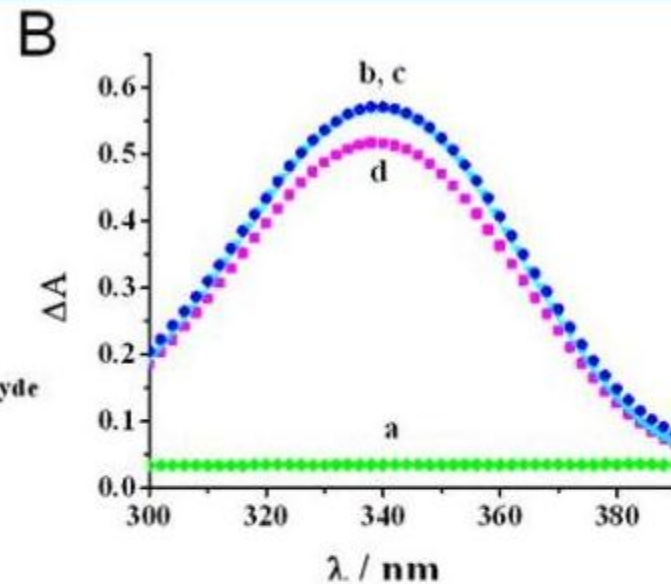
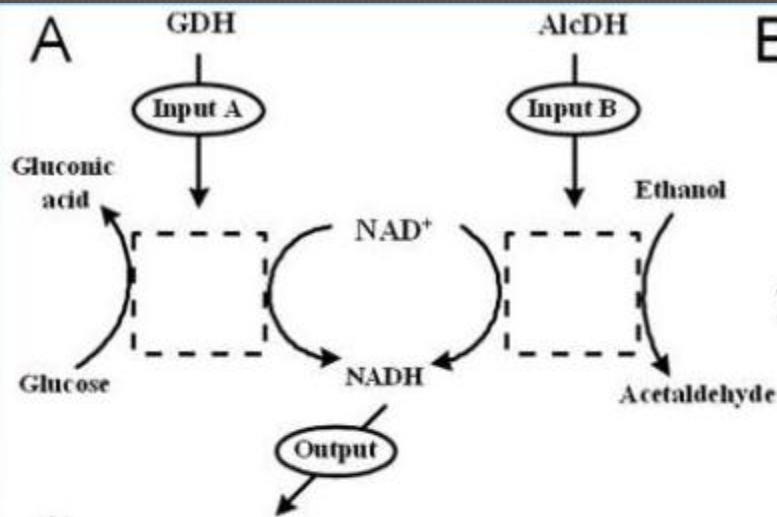


# OR Gate

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- ⦿ Solution containing **glucose, ethanol, and  $NAD^+$** .
- ⦿ Absorbance  $\lambda = 300 \sim 370 \text{ nm}$

# OR Gate



**D**

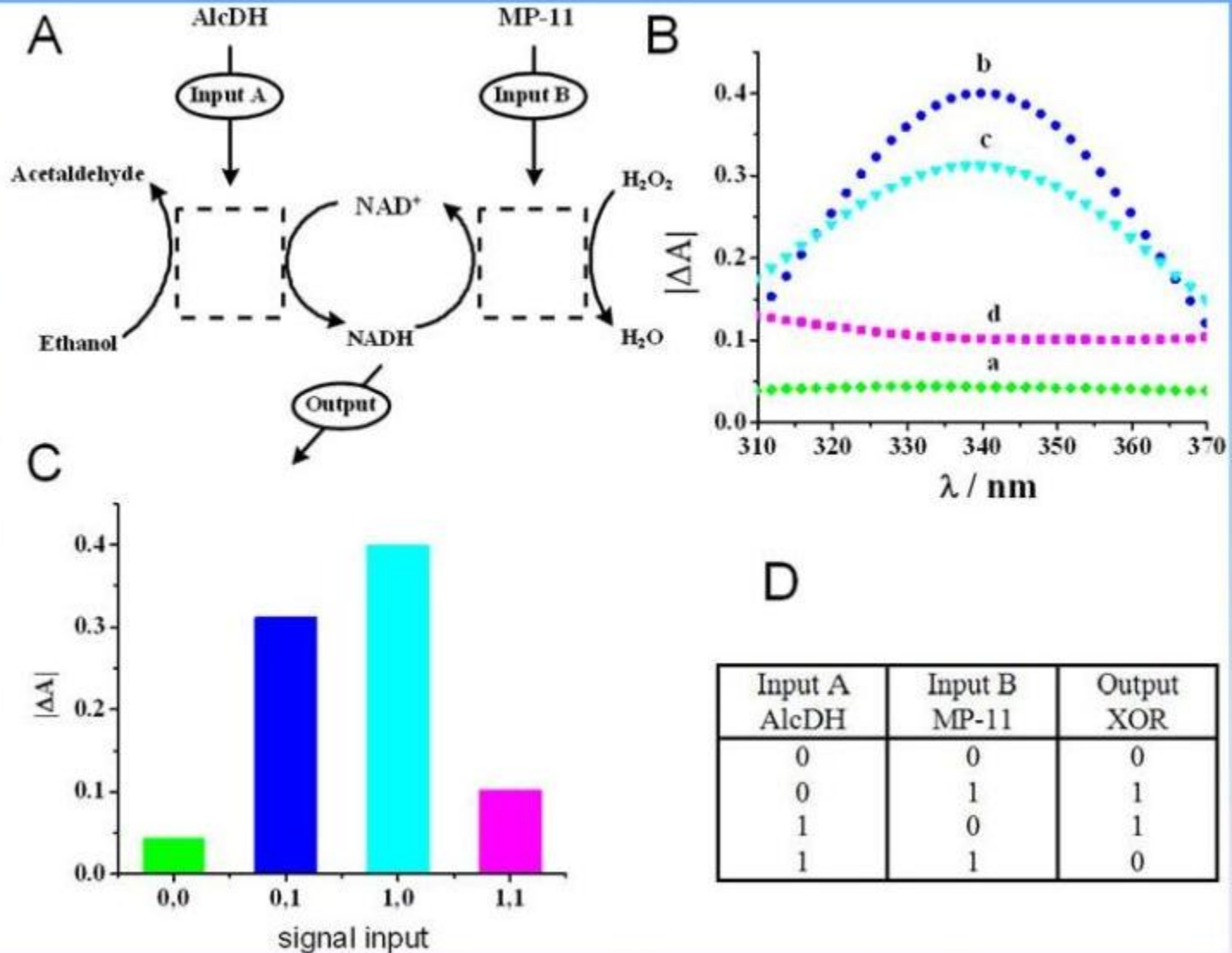
Input A AlcDH	Input B GDH	Output OR
0	0	0
0	1	1
1	0	1
1	1	1

# XOR Gate

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- ⦿ Solution containing  $H_2O_2$ , ethanol, NADH, and  $NAD^+$ .
- ⦿ Absorbance  $\lambda = 300 \sim 370 \text{ nm}$

# XOR Gate

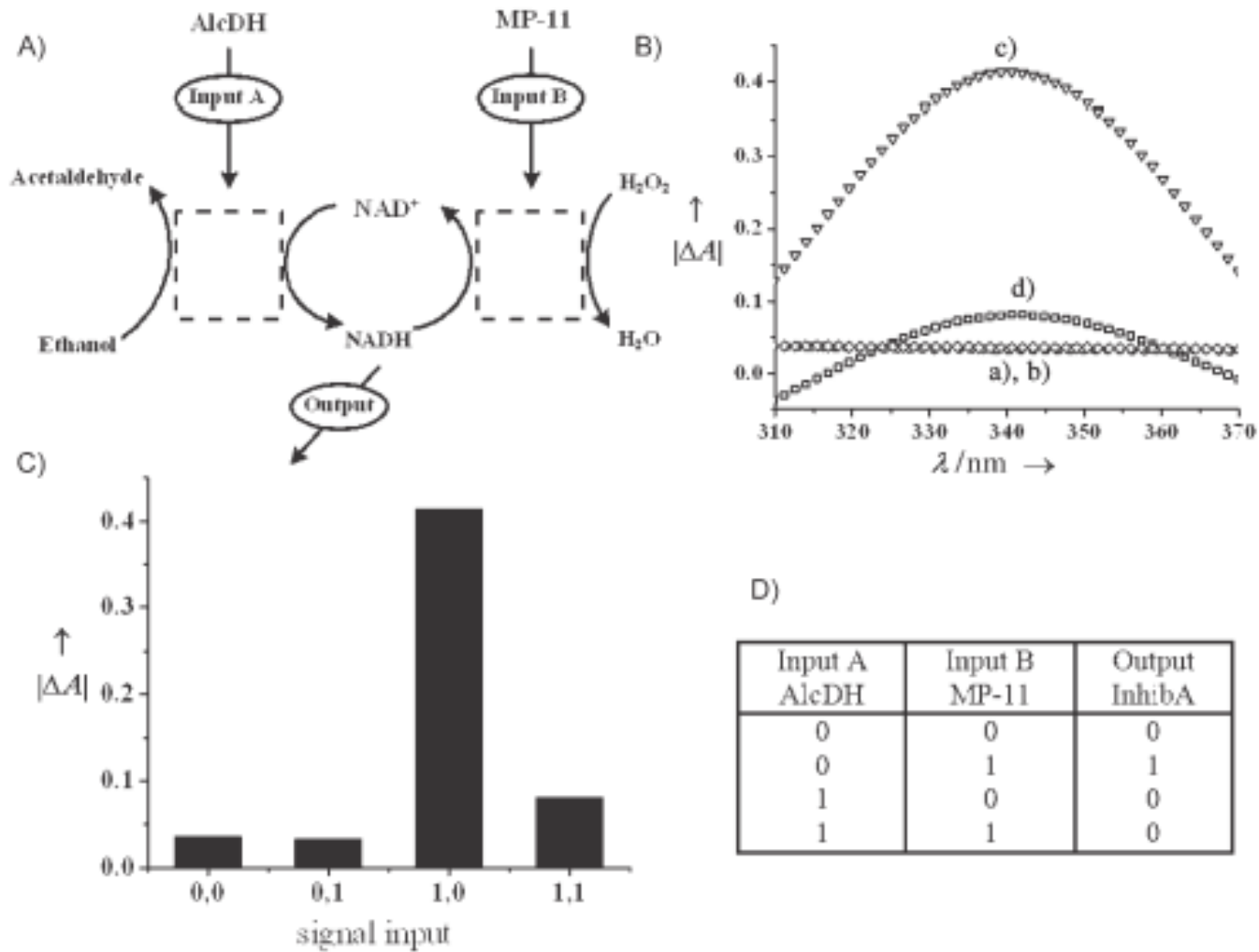


# InhibA Gate

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- ⦿ Solution containing  $H_2O_2$ , ethanol, and NADH.
- ⦿ Absorbance  $\lambda = 300 \sim 370 \text{ nm}$

# InhibA Gate



# Inverter

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- ◉ NOR, NAND

- ◉ Using different AND & OR

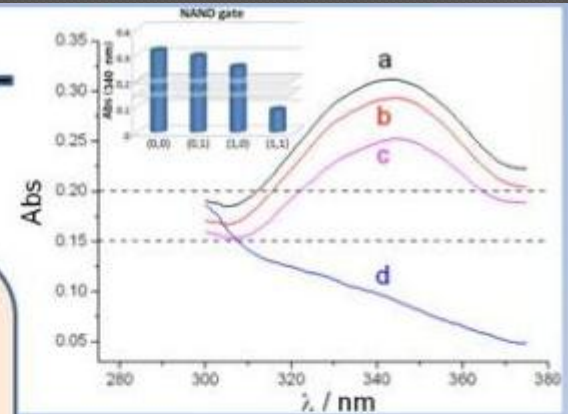
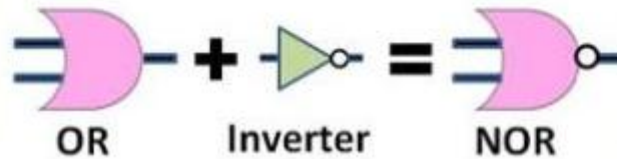
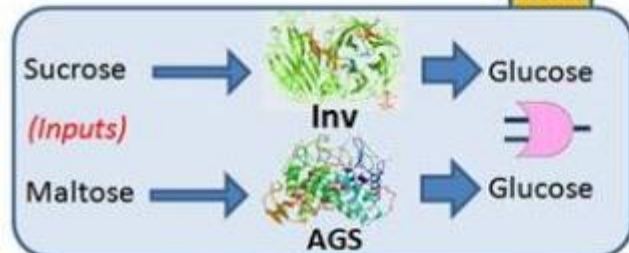
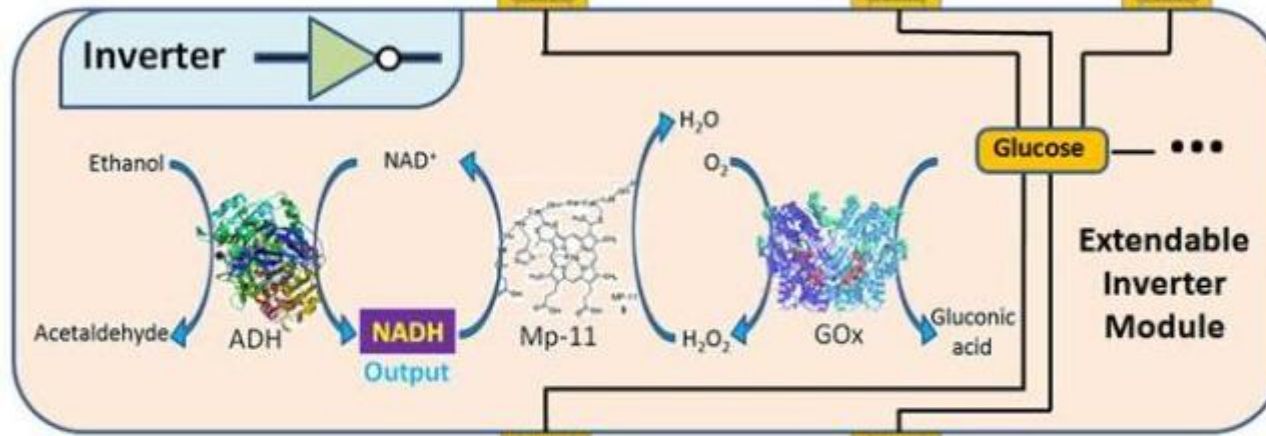
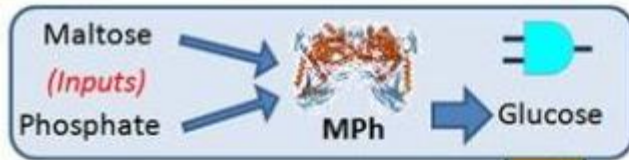
# Inverter

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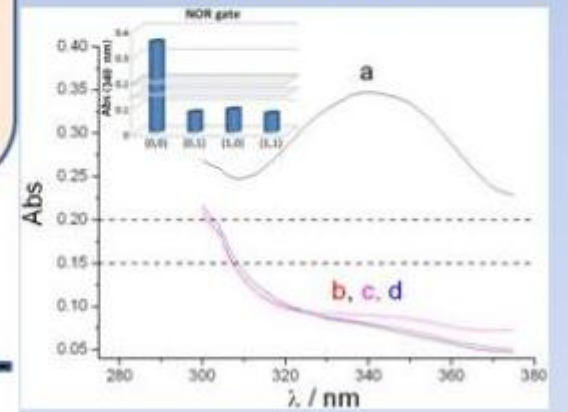
- ◉ AND : MPh (maltose phosphorylase)  
pH 7.2, HEPES buffer
- ◉ OR : Inv (invertase)  
AGS (amyloglucosidase)  
pH7.2, phosphate buffer
- ◉ Inverter : ADH, GO<sub>x</sub>,  $NAD^+$ , MP-11  
ethanol



# Inverter



NAND gate



NOR gate

# Filter

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- ◉ Become more complicated → high noise level
- ◉ Concentration
- ◉ Negative catalyst
- ◉ *HRP*,  $H_2O_2$ , TMB, **Ascorbate**

# Filter

Input :  $H_2O_2$

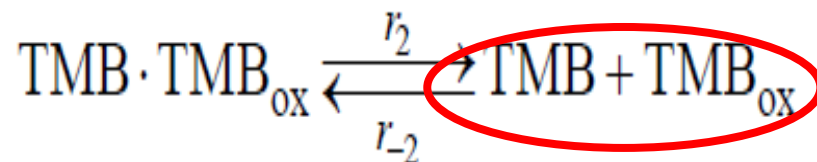
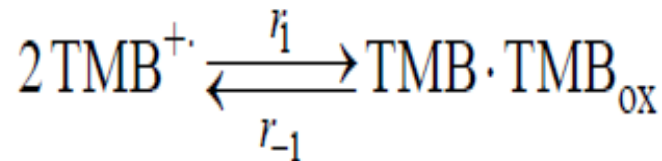
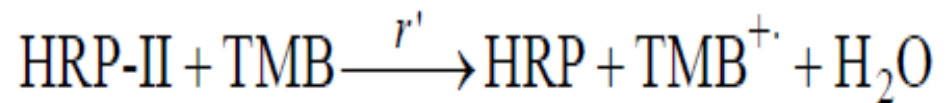
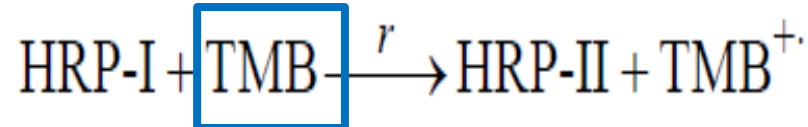
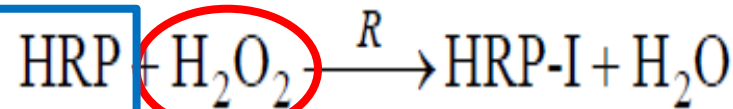
Catalyzed by HRP

Output :

TMB and  $TMB_{ox}$

→ blue

Convex function :  
small input can still  
cause saturation



# Filter

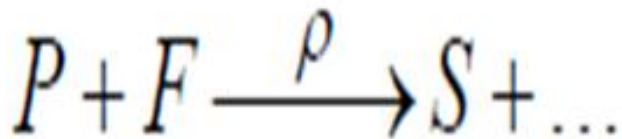
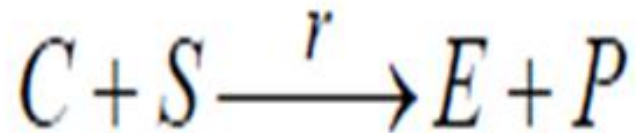
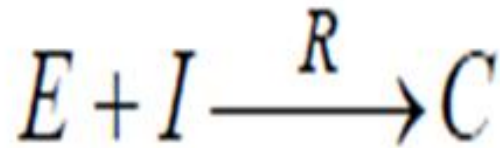
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⊙ F : neutralize output

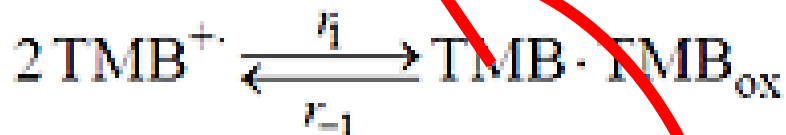
⊙ Ascorbate (ASC)

⊙ Small input :  $P \rightarrow 0$

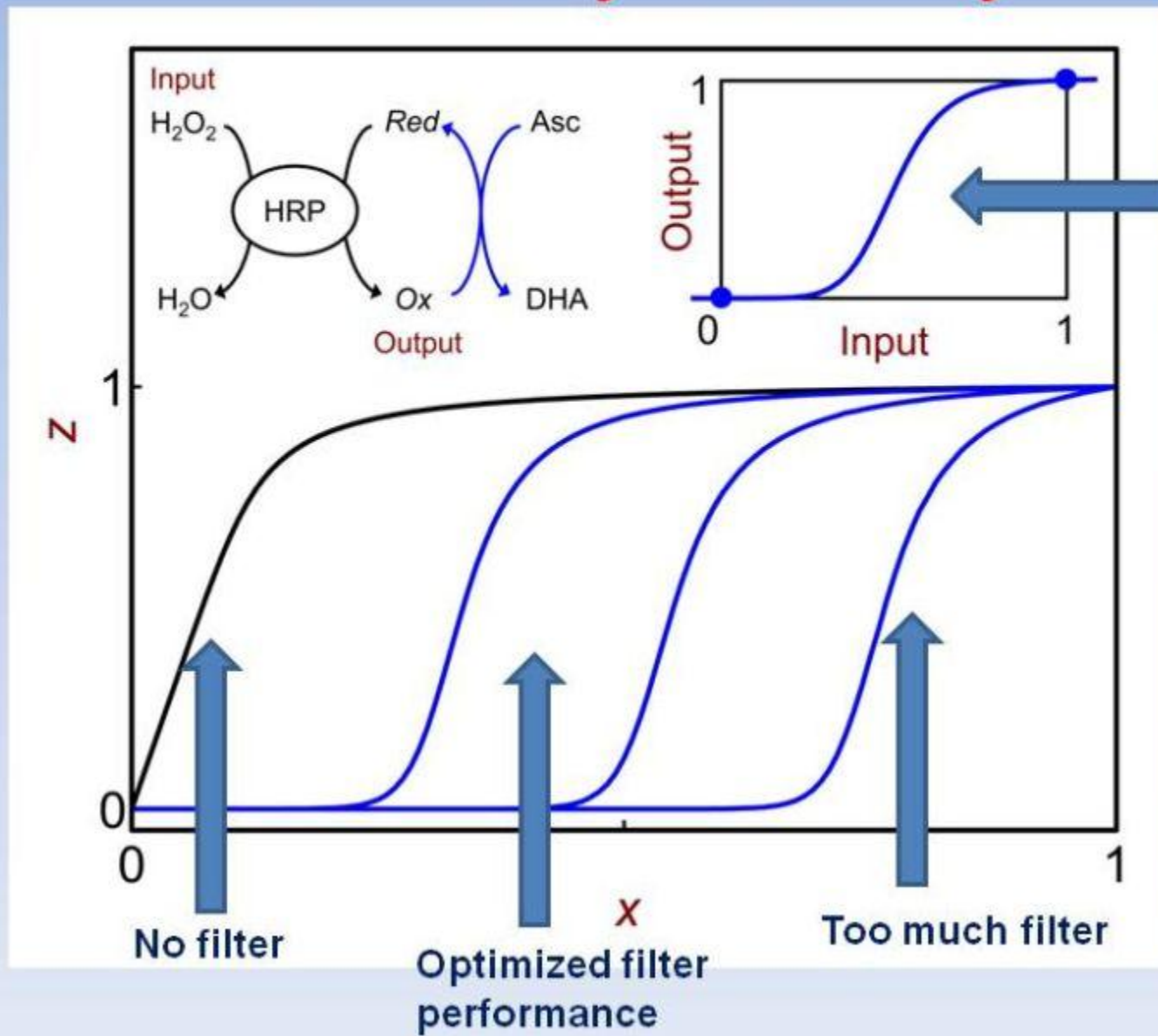
Large input :  $P \rightarrow 1$



# Filter



# Chemical “filter” system for reduction of noise in enzyme-based systems



# Filter

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- ◉ Buffer
- ◉ Ethyl butyrate(丁酸乙酯) → butyric acid(丁酸)
- ◉ Measured by the drop in the pH value.
- ◉ Esterase(酯酶)當催化劑

# Filter

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- ⦿ Small input → HEPES(buffer) consumes most of the  $H^+$
- ⦿ Large input → produced  $H^+$  ions overwhelm the buffer



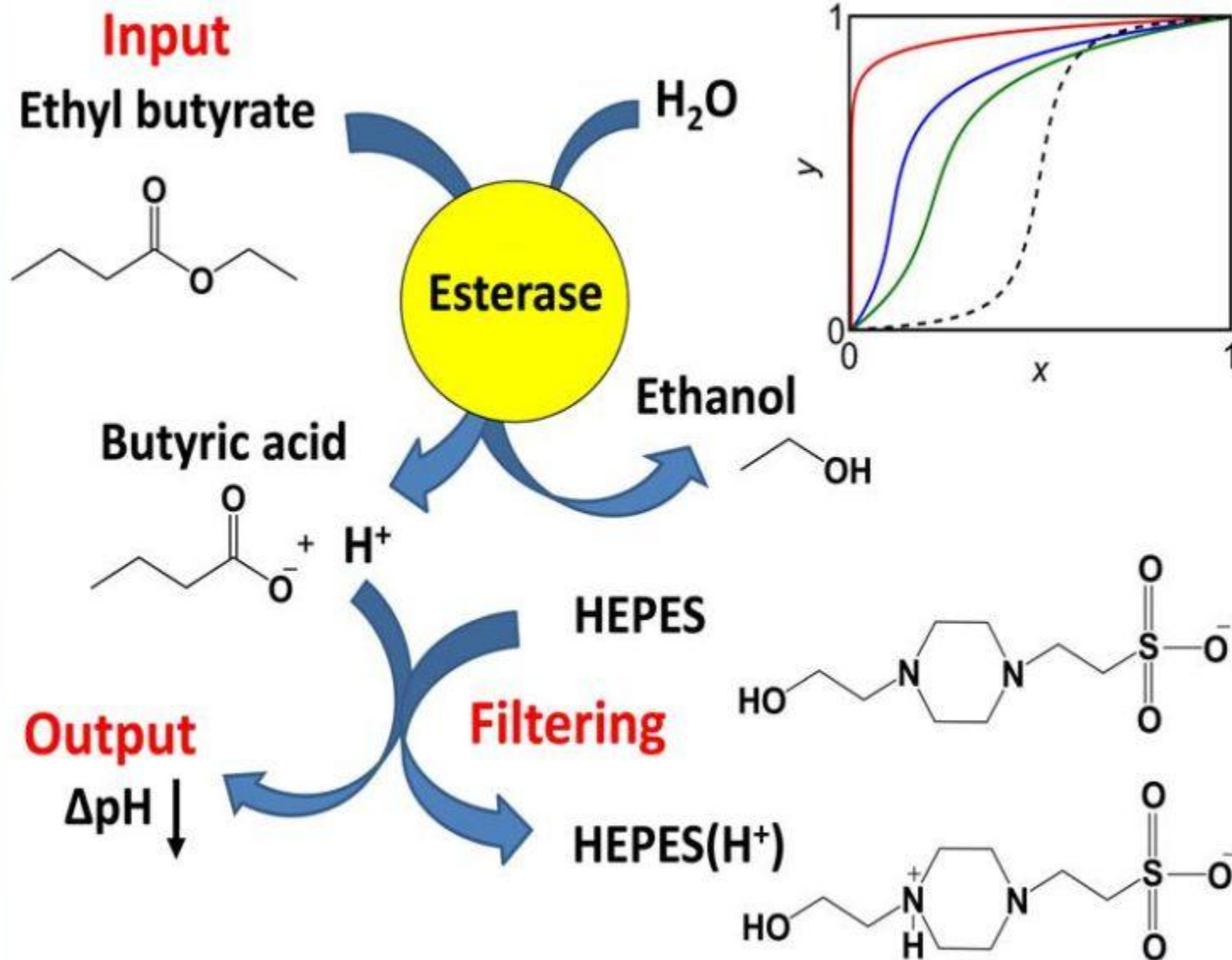
# Buffered Biocatalytic Signal Transduction



Dr. Marcos Pita



Mary A. Arugula,  
PhD student



# Signal Amplifier

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- Use ADH as the biocatalyst to produce NADH with the presence of  $\text{NAD}^+$  and ethanol.
- The process must be activated by NADH signal.

# Signal Amplifier

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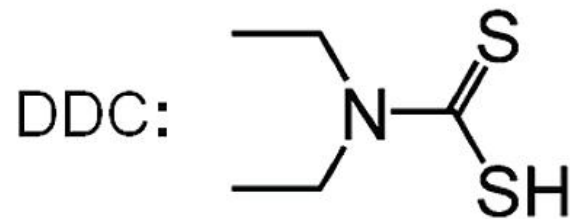
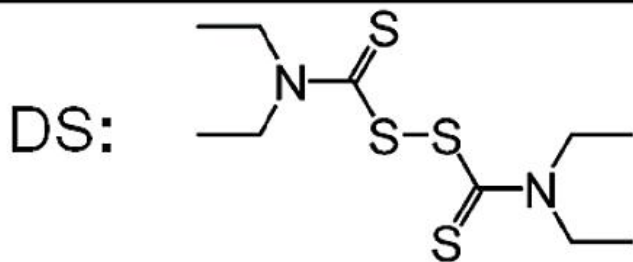
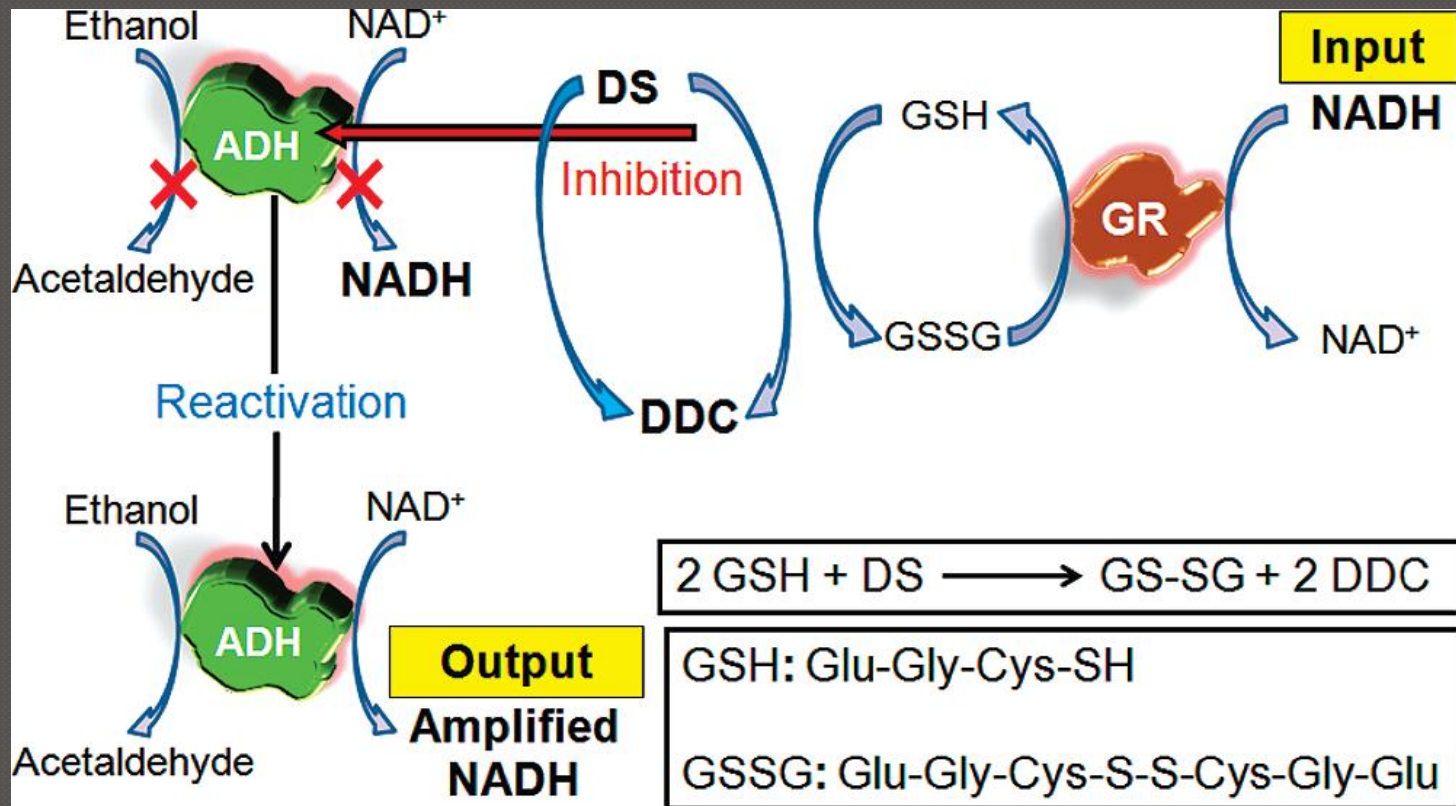
- Use DS to inhibit ADH.
- Need a system to remove the inhibitor that initialized by NADH.

# Signal Amplifier

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- GSH can reduce DS and oxidized to GSSG .
- With presence of NADH and GR, GSSG reduced to GSH.

# Signal Amplifier



# Signal Amplifier

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- ◉ Concentration of DS must be optimized
- ◉ Lower: No substantial inhibition of ADH
- ◉ Higher: Not allow the enzyme reactivation

# Signal Amplifier

