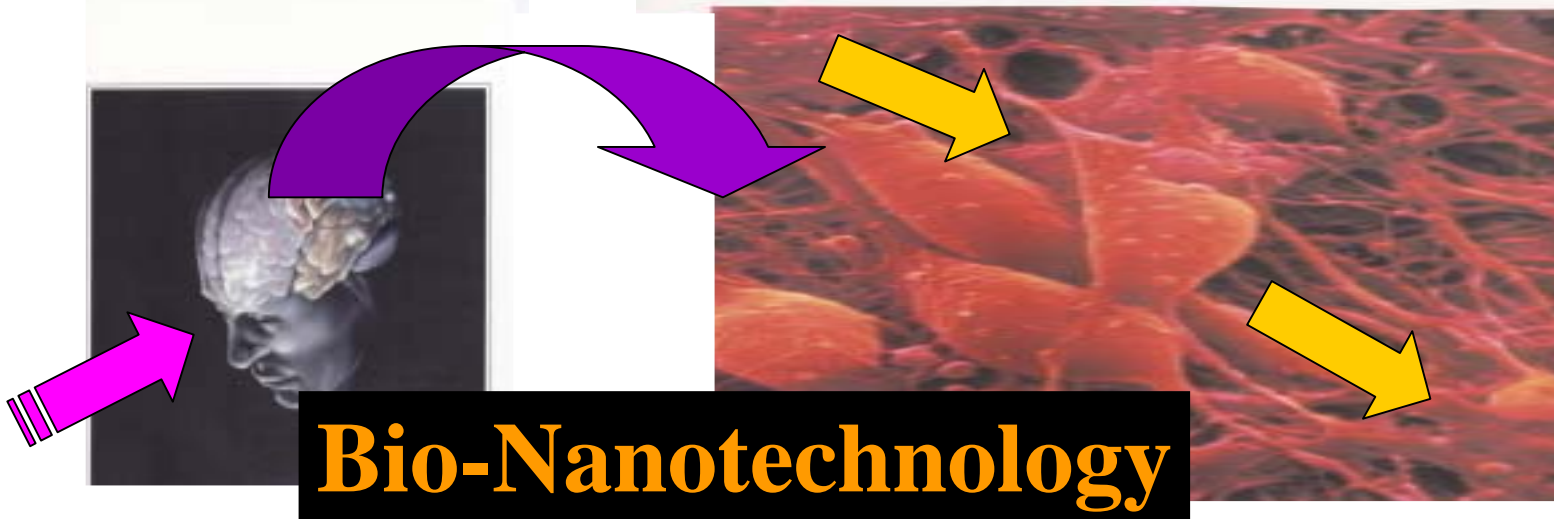


# Challenges of Bio-Nanotechnology

**Masuo Aizawa, President  
Tokyo Institute of Technology, Tokyo**



# *Explore the Biological Information World*



**Stimulation**

## **Biological Information World**

### **Inter-cellular Information Networks**

Brain, Sensory, Nerve, Immune, and Excretory Systems

### **Intra-cellular Information Networks**

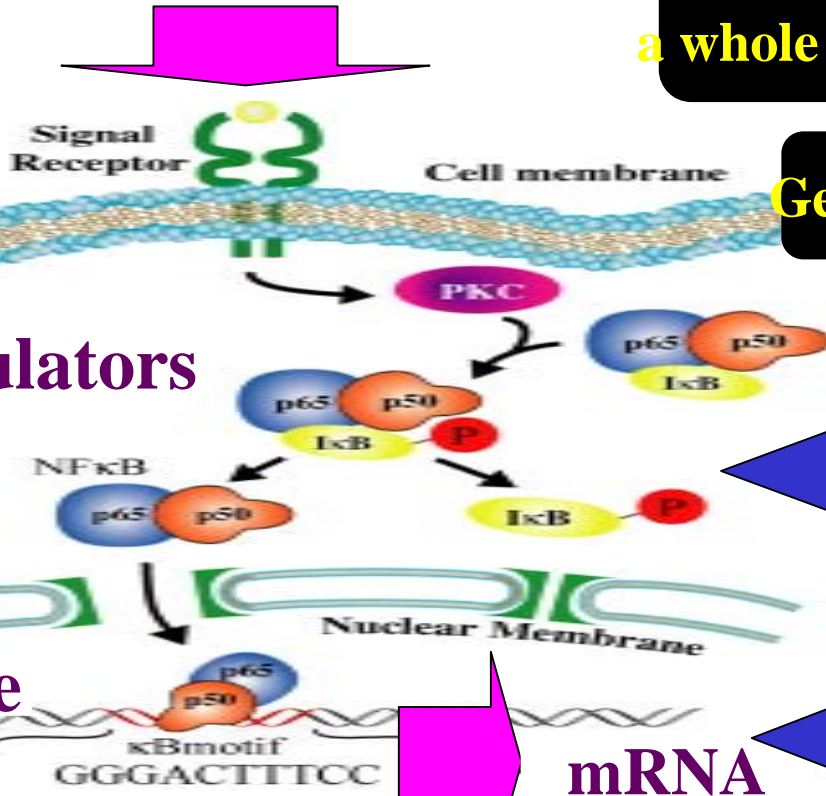
Signal Transducing Networks, Genome Networks

# Nanotechnology Unveils How Biological Information Is Processed

Input Signal

A cell is a minimum unit of life, containing a whole set of information networks.

Gene Information is stored in DNA.



Regulators

Signal Transduction

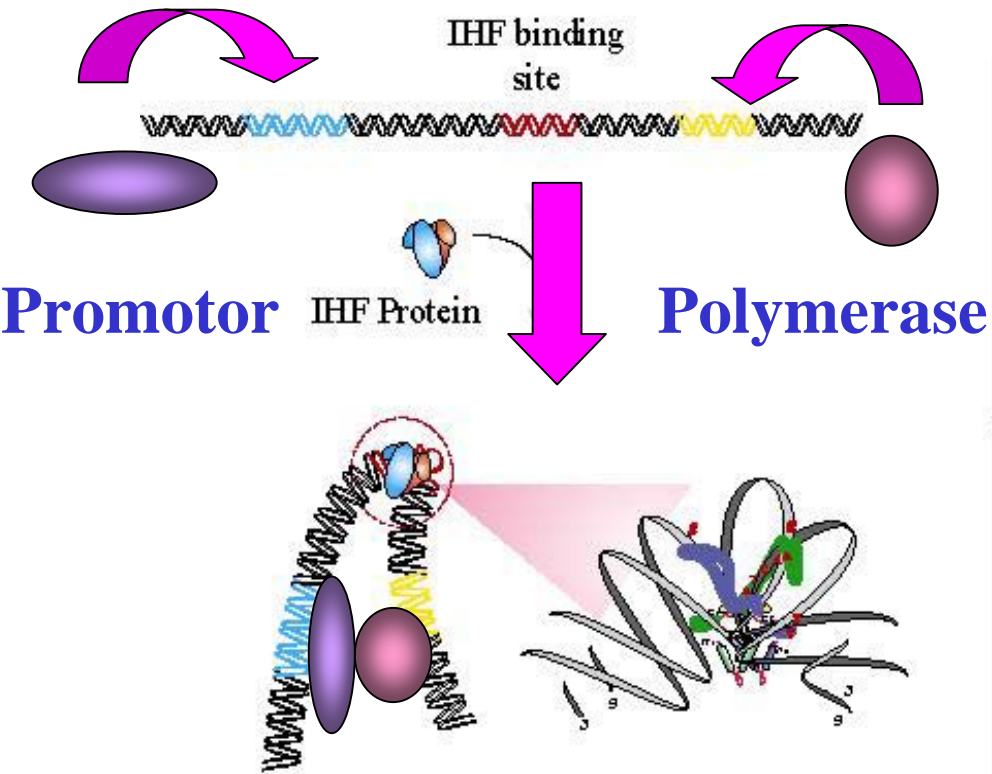
How ?

Gene Expression

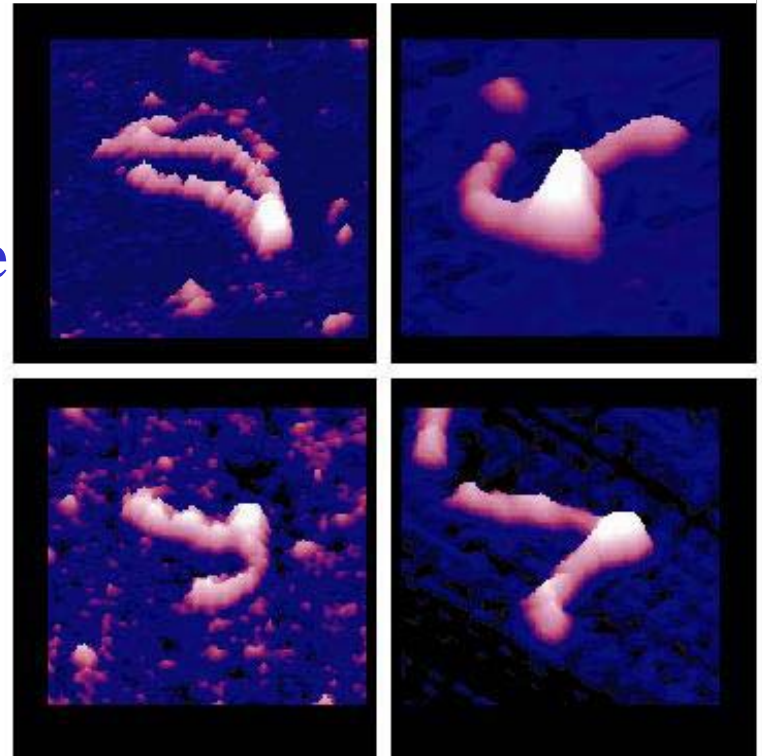
Transcription

When ? How ?

# DNA Nano-structure Change Proven in Transcription by Single Mol. AFM Imaging

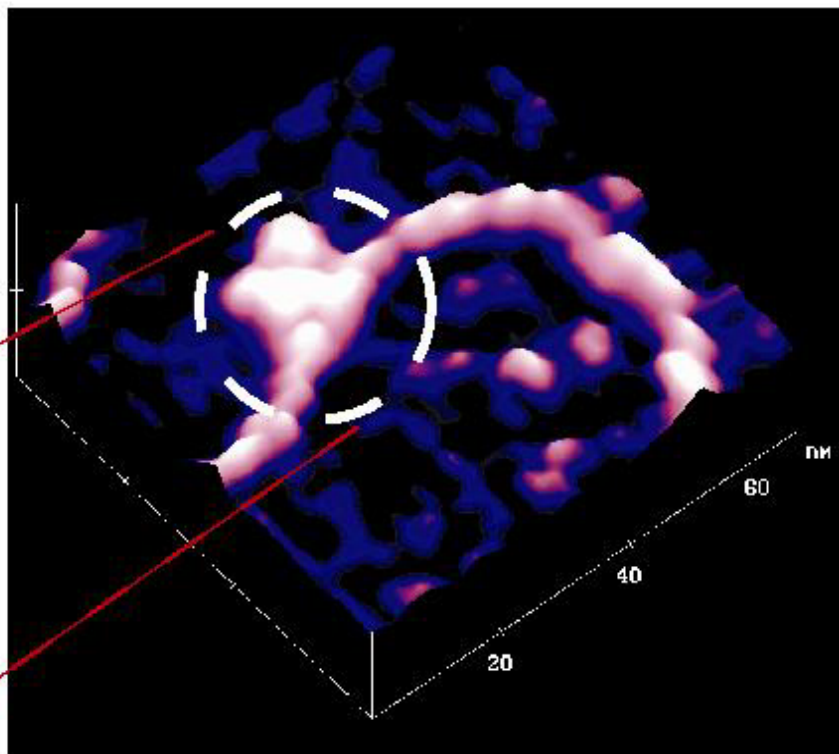
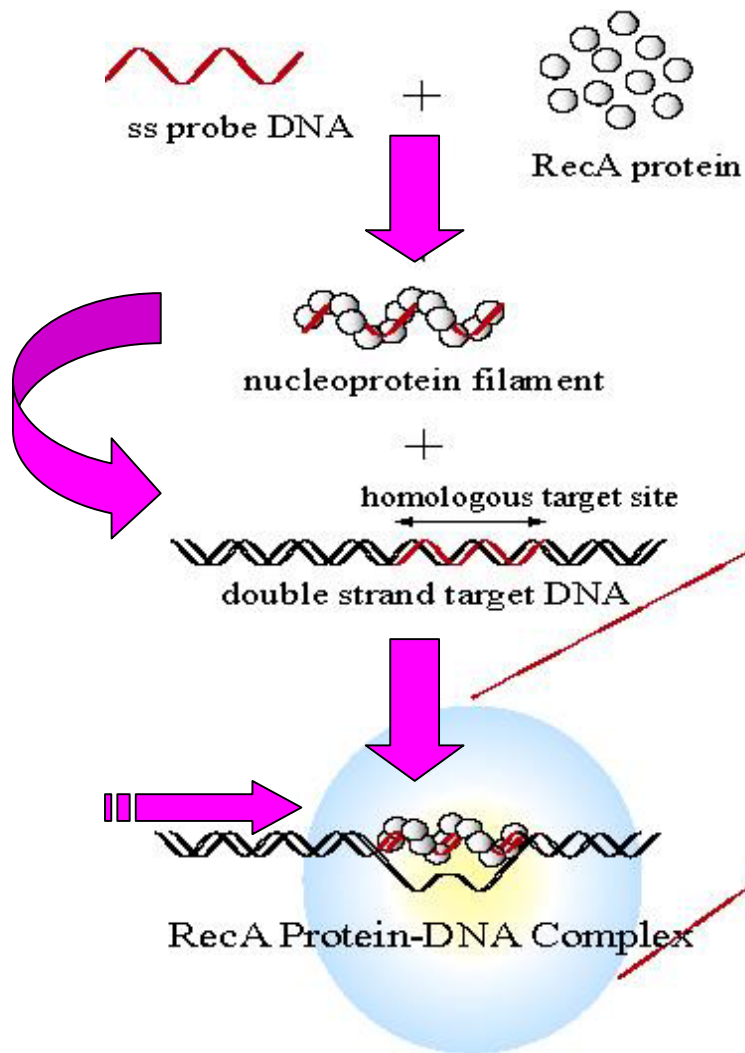


## AFM Imaging of DNA



Biochem. Biophys. Res. Commun., 291, 361-366 (2002)

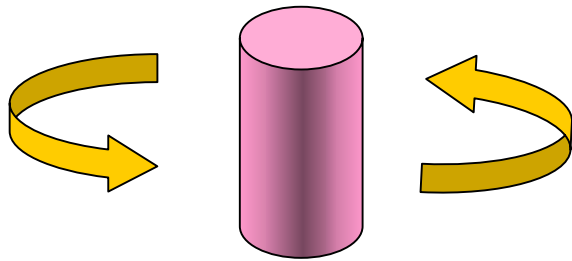
# RecA Protein Slides along a DNA Chain



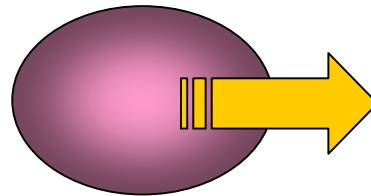
Anal. Chem., 72 (6), 1288-1293 (2000)

# Biological Information Processed by Nano-structure Changes of Molecules

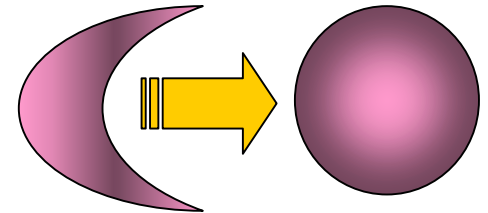
Molecular Rotation



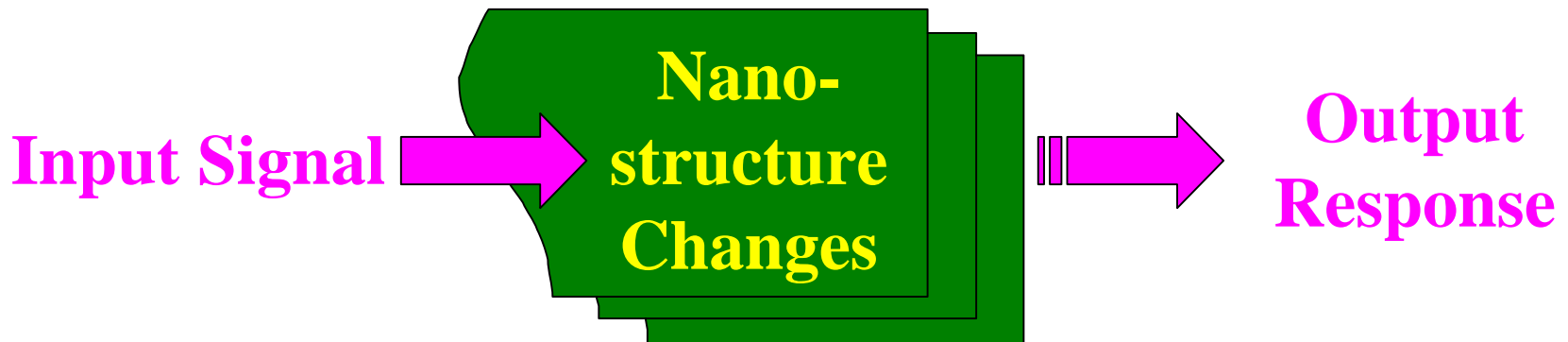
Translation



Conformation Change



*Molecular Computing !*



*Different from Electronic Computing*

# *Where to go ?*

## *Bio-Nanotechnology Measurements*

*From in vitro to in vivo !*

**Dynamic Mol. Interaction**

**3D Molecular Imaging**

**Single Molecule Detection**

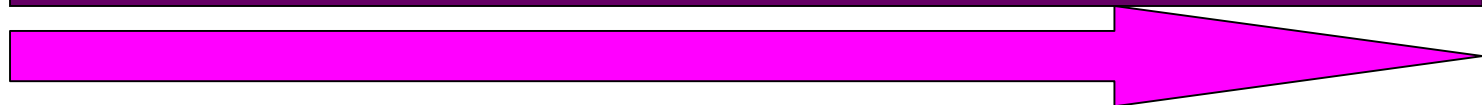
**Molecular Networks  
in a Living Cell**

**DNA, Mol.motor**

**Genomics**

**Proteomics**

**Cell Biology**



# Challenging Physical Control of the Biological Information Processing

**Physical Input Signals**

Electric stimulation

Mechanical

Magnetic

Molecular Information  
Networks

**Nano-structure Changes**

**Cell Growth**

**Gene Expression**

**Cell Differentiation**

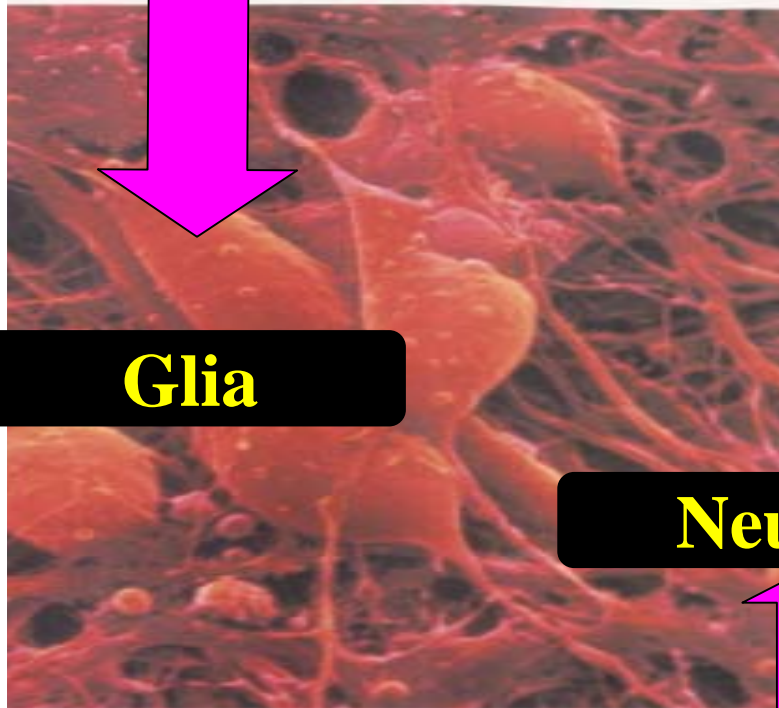
*Physical Control  
of Life !*

# Discovery of Electrically Controlled Gene Expression in a Living Cell

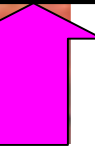
Electric stimulation



Glia

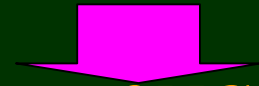


Neuron

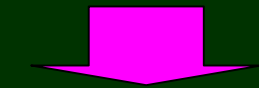


Excreted Nerve Growth Factor (NGF)

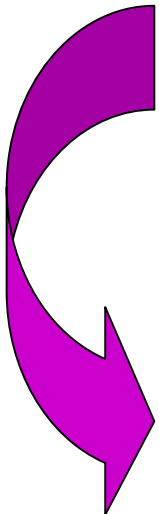
NGF gene at resting stage



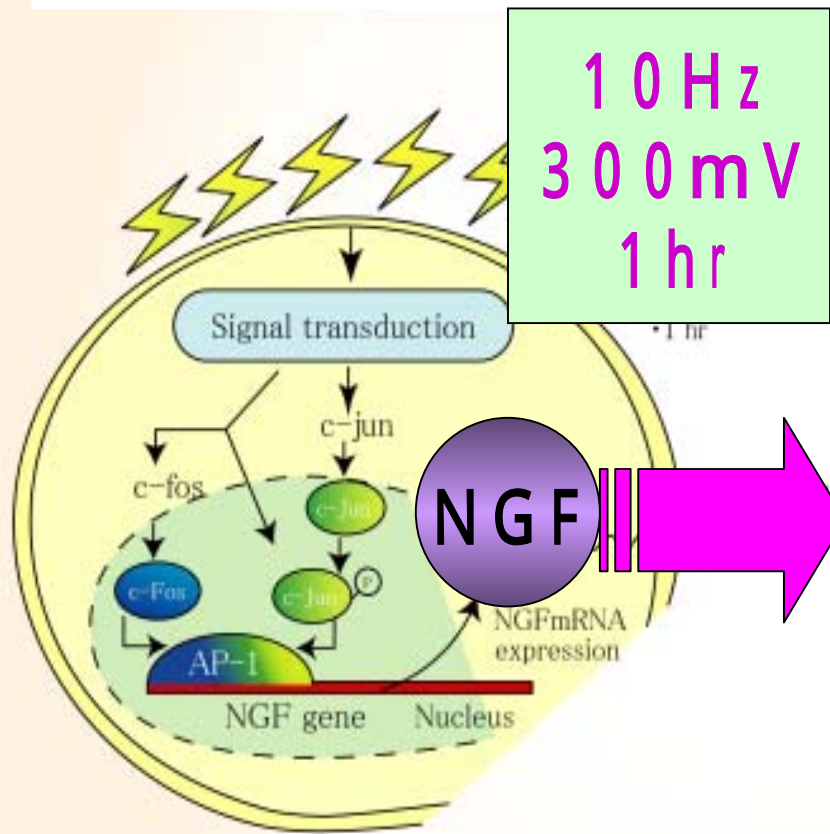
Activation of NGF gene  
Expression by Electric  
Stimulation



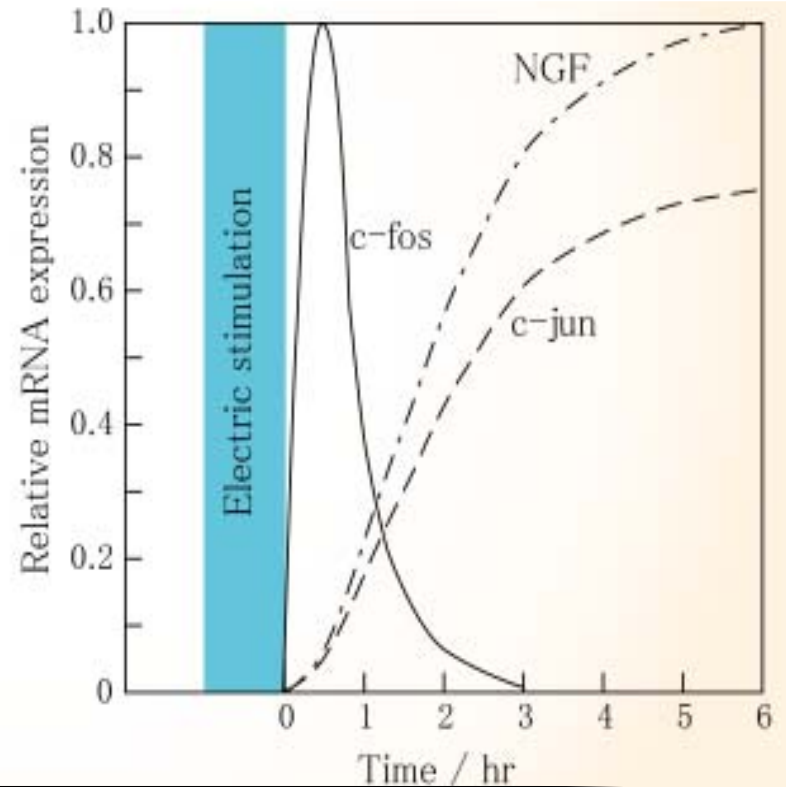
Excretion of NGF



# NGF Gene is Electrically Activated



Nature Biotech., 15, 164 (1997)



NGF Gene

NGF mRNA

NGF

# Postulated Cellular Response Mechanism

**Electric stimulation**

**SA-channel**

**PLC**

**PKC**

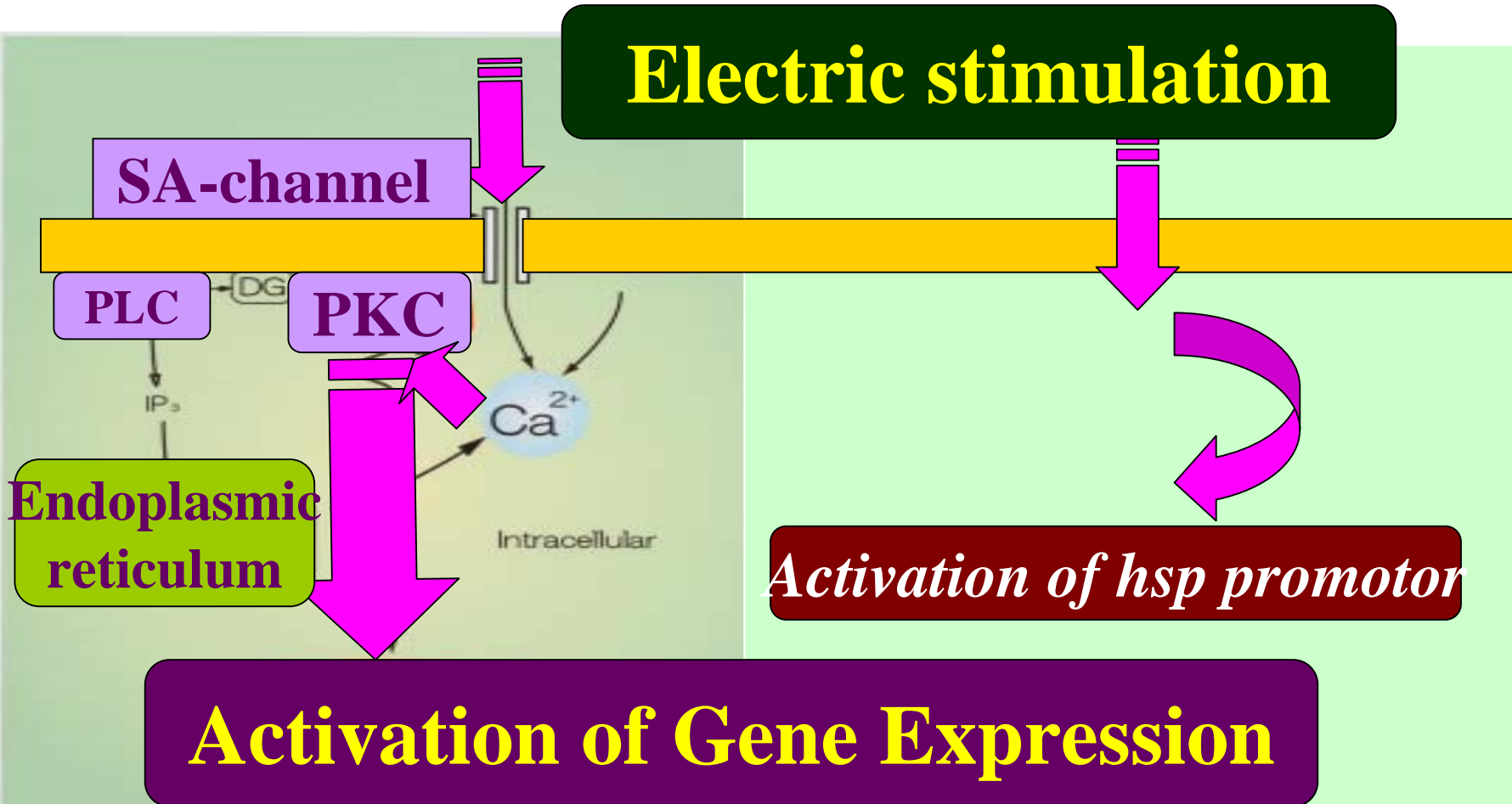
$\text{Ca}^{2+}$

**Endoplasmic  
reticulum**

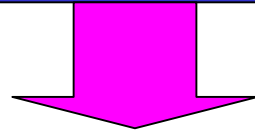
Intracellular

*Activation of hsp promotor*

**Activation of Gene Expression**



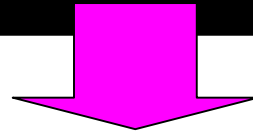
**Physical Stimulation**



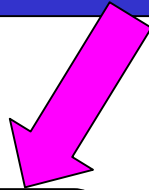
*Biological  
Information  
Networks in a  
Living Cell*



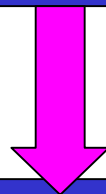
**Nano-structure Changes**



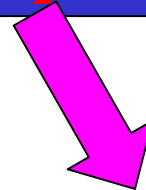
**Activation of Gene Expression**



**Proliferation**



**Protein  
Synthesis**



**Differentiation**