

Physical Controls of Nano-structures in the Biological Information Processes

- 1. Discovery of Electric Activation of Gene Expression**
 - 1) Electrically Induced Nano-structure Changes**
 - 2) Electrically Responsive Gene**
- 2. Electrically Directed Gene Expression**
 - 1) Switching ON and OFF**
 - 2) Site-directed Switching ON and OFF**
- 3. Electric Control of Cellular Activities**
 - 1) Electrically Induced Differentiation**
- 4. Perspectives of Electrically Responsive Cells**
 - 1) Pancreas Alternative for Excreting Insulin**
 - 2) Electrically Controlled DDS on Demand**

Background of Bio-devices R & D

1. Biosensor Technology in 1970's and 1980's

- 1) Enzyme sensors : Updike and Hicks (1964)
- 2) Immunosensors : Aizawa and Suzuki(1974)
- 3) Successful R & D of Biosensors

2. Bio-device Initiatives in 1980's and 1990's

- 1) MITI Project Directed by Aizawa
- 2) From “Biochip” to Generic Technology

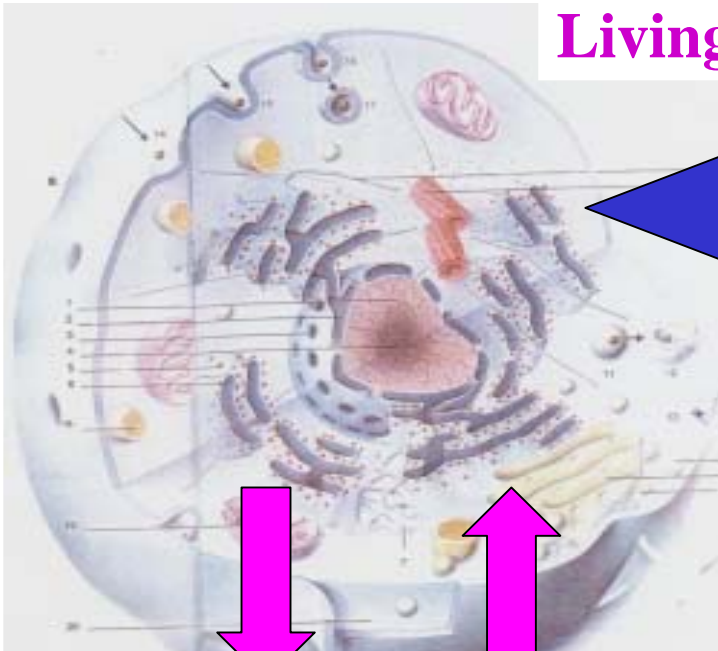
3. DNA Chips in mid 1990's

- 1) Integrated Technologies
- 2) Demand for Genome Analysis

4. Towards Nanotechnology-Based Bio-devices

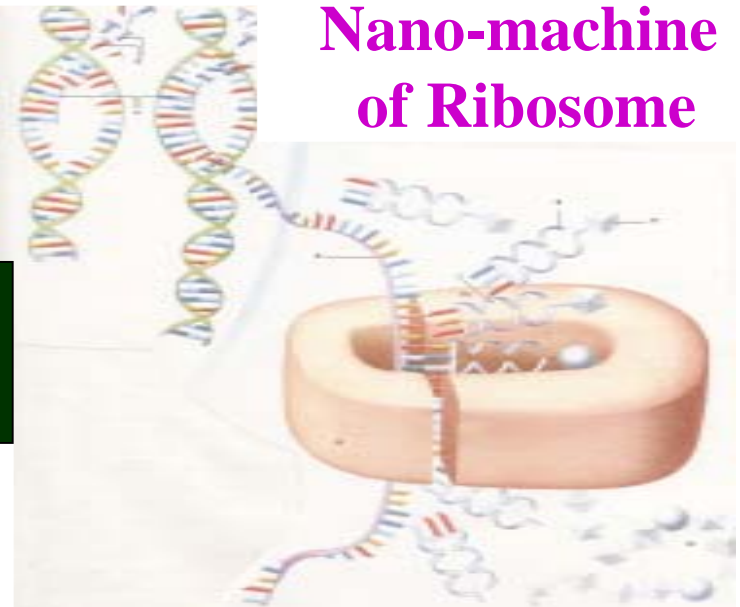
Towards Nanotechnology-based Bio-devices with the Biological Information Systems

Living Cell



**Use of Total Biological
Information System**

**Nano-machine
of Ribosome**



Bio-interface



Ultimate Bio-devices : *What's for ?*

1. Medical Bio-devices for Therapeutics

- 1) Drug Delivery System (DDS) with Living Cells**
- 2) Pancreas Alternative with Living Cells**

2. Medical Bio-devices for Health Care

- 1) Biochemical Diagnosis for Personal Use**
- 2) Gene Diagnosis**

3. Bio-devices for Safety Care

- 1) Safety Assessment of Chemicals and Foods**
- 2) Security Checks**

4. Bio-devices for Drug Discovery

- 1) Screening Drug Candidates**
- 2) Animal Test Alternative**

Cellular Devices for Pancreas Alternative

Electrically Responsive
Insulin Gene

*Insulin Production is
Electrically
Switched On and Off.*

**Programmed
Electric
Direction**



**Insulin
Excretion**

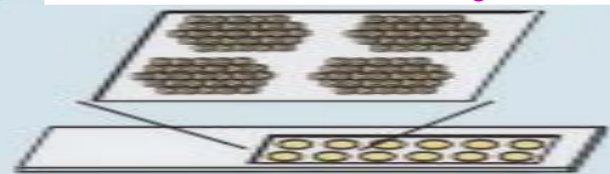
Genetically Engineered Cell

Cellular Bio-devices for Safety Check

Engineered Cell



Cell Array



Cell Responses

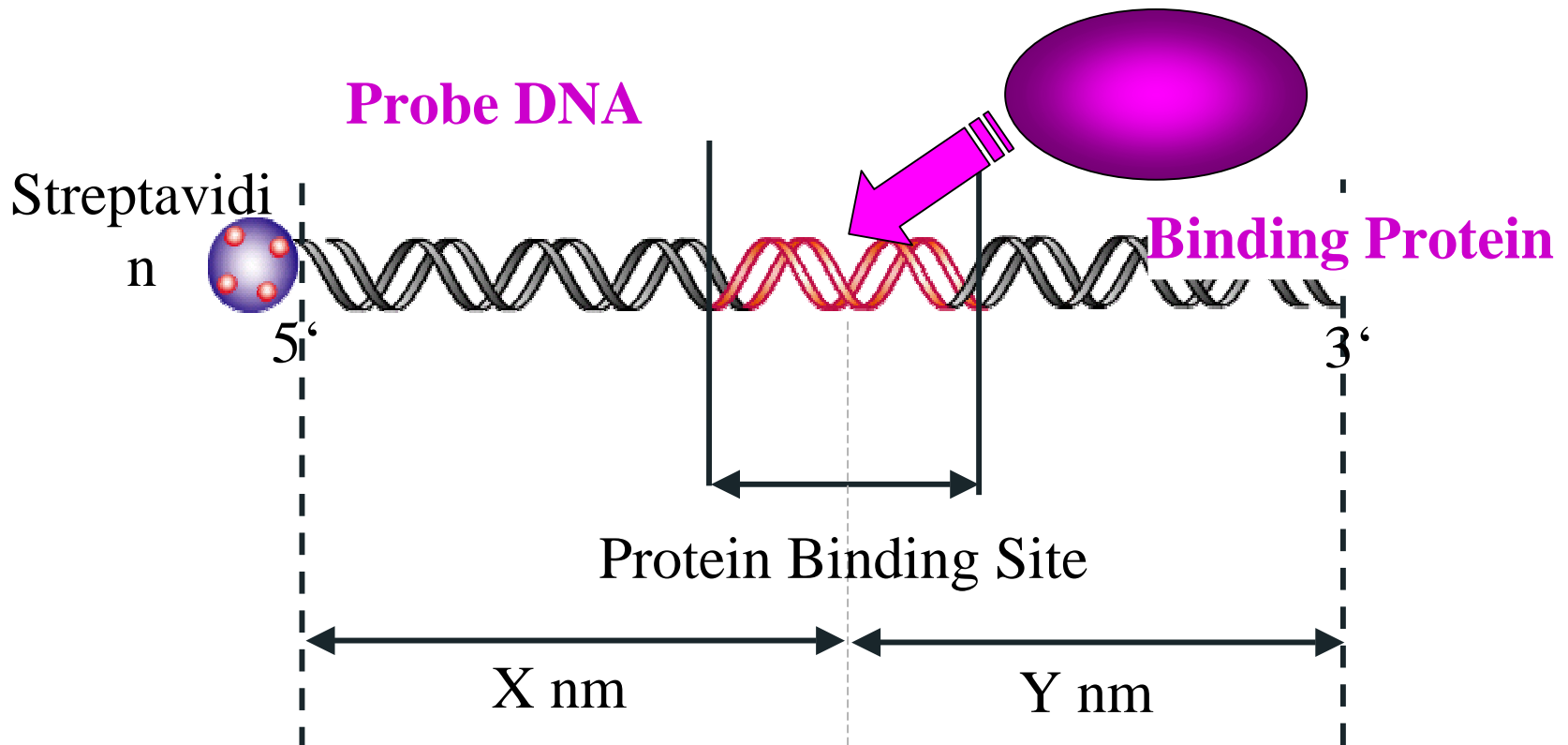
Safety Check

Toxic?

Genetically Safe?

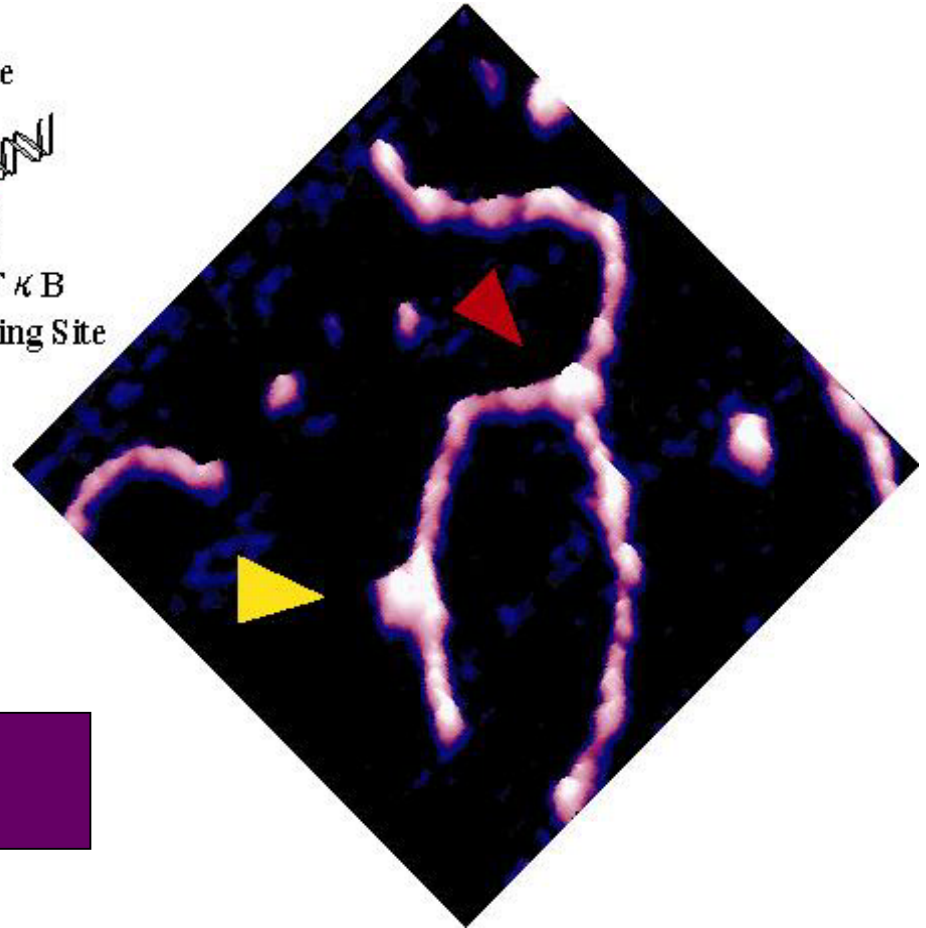
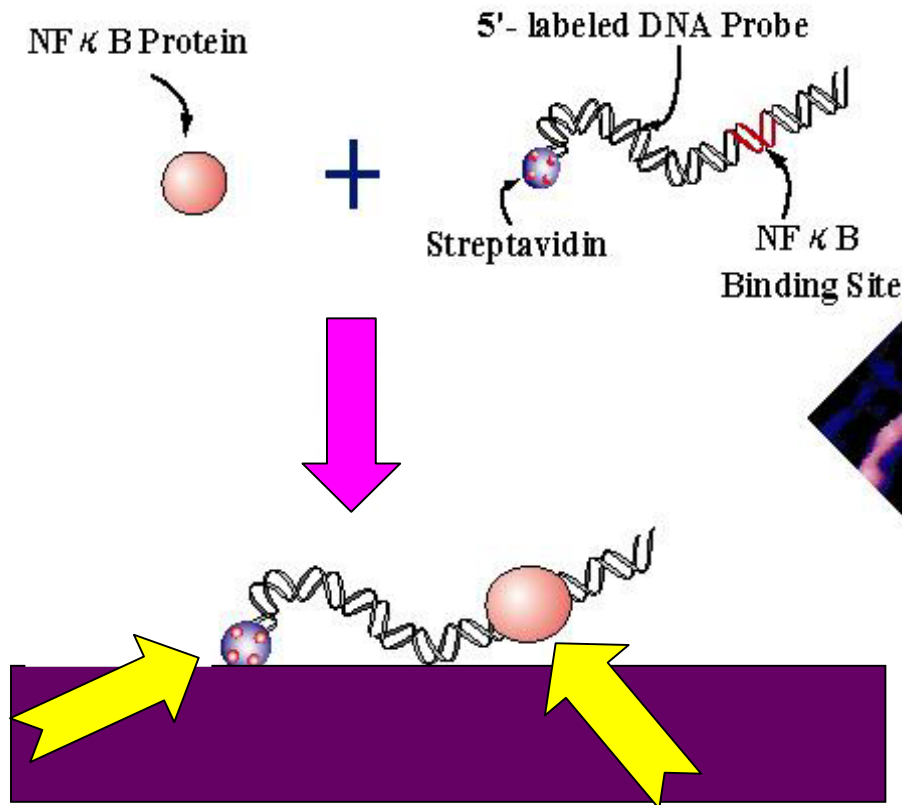
Toward Animal Test Alternatives

Single Molecule DNA Bio-device for Drug Discovery



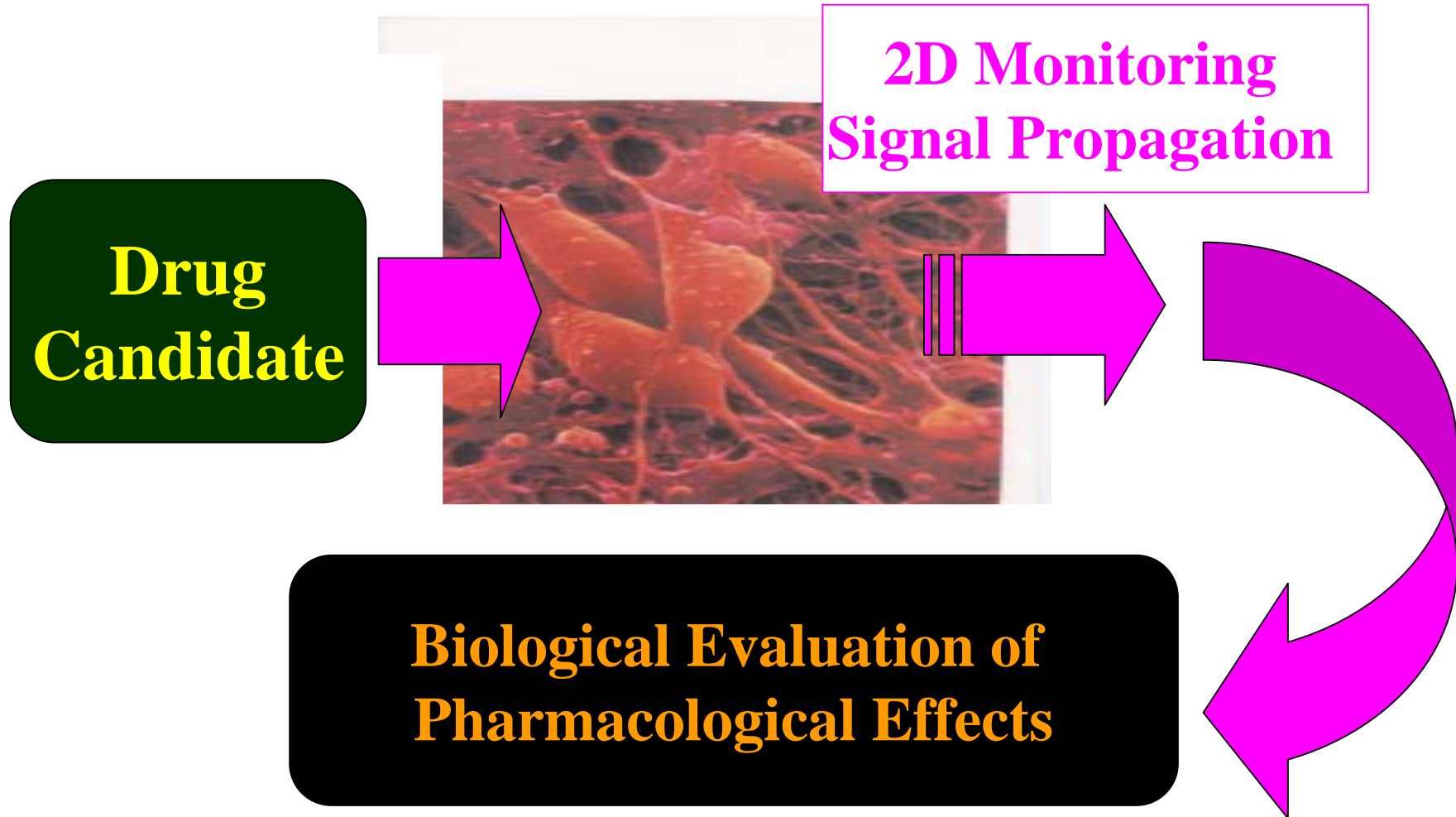
Picking up a Single Molecule from Cell Lysate !

Individual Molecule Is Selectively Fixed

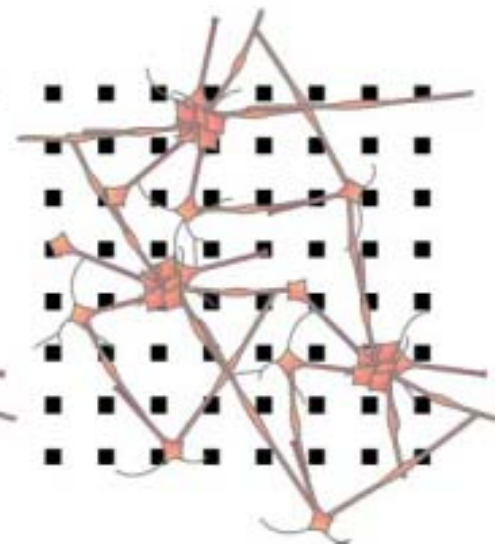
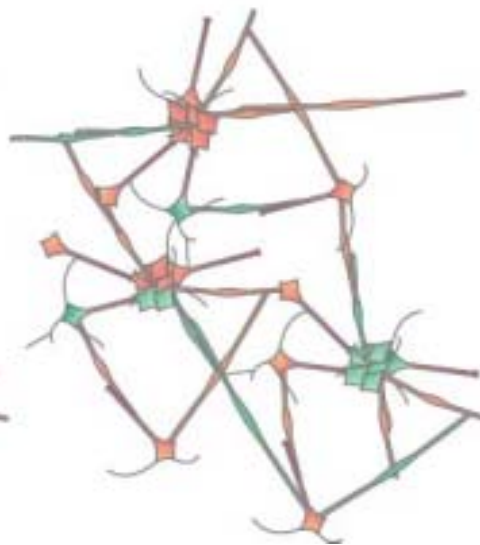
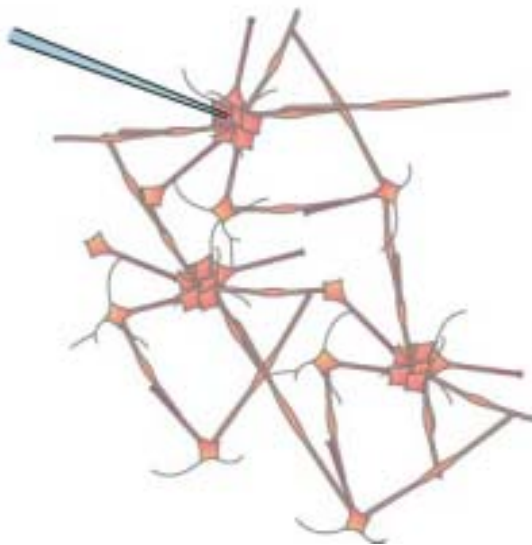
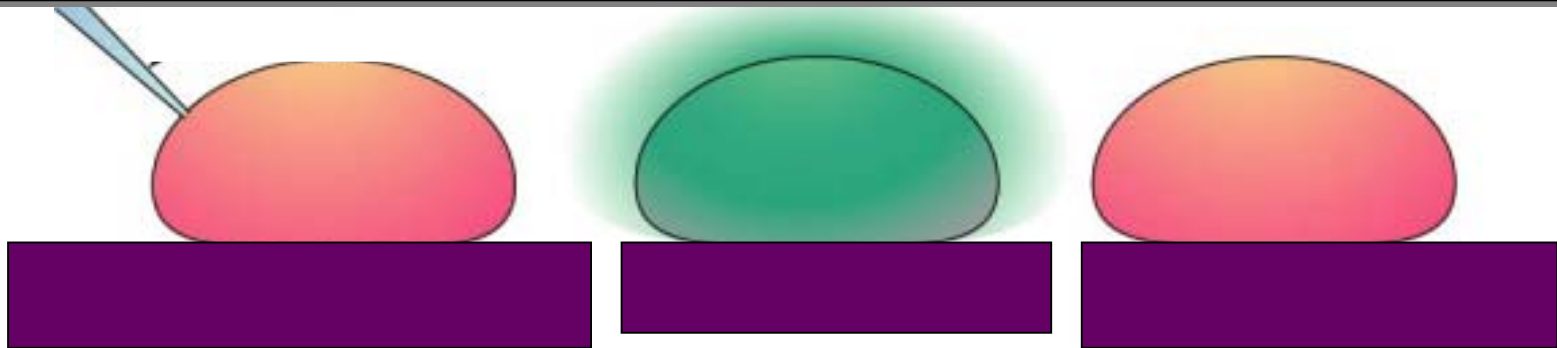


Anal. Biochem., 309, 241-247 (2002)

Animal Test Alternative for Biological Evaluation



Biological Evaluation by Monitoring Neuro Network Signal Propagation



Patch Clump

2D Optical

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Electrode Array

Medical Application Perspectives of Bio-devices

Health Care

Safety Check

Pancreas Alternative

Drug Discovery

Genomics, Proteomics

Drug Delivery

Bio-devices for

Single Mol.Det.

Massive Inform.

Biol.Inform.Networks

Nano-Probing

Cellular Bio-devices

Protein Chips

Micro-TAS

Bio-MEMS

Biosensors

DNA Chips

Micro-fluidics

Conclusion

- 1. Bio-nanotechnology opened a door to the Biological Information World.*
- 2. Biological information is processed through the Nano-structure Changes.*
- 3. Electrically controlled biological information has been accomplished.*
- 4. Nanotechnology-based bio-devices and bio-systems are promising.*