Chemistry, What's Next?:

Studies on Fundamental Principles for life

2019.6.13

전승준
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子曰 學而時習之면 不亦說乎아

공자께서 말씀하시길
“배우고 때때로 익히면 기쁘지 않겠는가”

- 論語(논어): 學而(학이)편-

Journey of My Quest in Science

爲人之學

81-84 Ion beam 실험 연구
(Laser spectroscopy)

84-86 Radical의 고압 안정화 연구
(Pressure-induced Solid state Phase transition)

86-88 고체수소 및 산소 고압연구
(Metallic Hydrogen, Bose-Einstein Condensation, Quantum Solid)

89-95 분광학과 고압, 계산화학

95-06 유기 비선형 광학물질연구 (조봉래교수님)
(2차 유기 비선형광학 물질, 이광자 형광 현미경)

98.3-99.2 UC Berkeley – Sabbatical (not Nano, rather Bio)

06-09 다차원 비선형 분광학(조민행교수님)

爲己之學 11-미래 Chemistry for Life

Chemistry, What's Next? (in 1990)

"What will Chemistry do in the Next Twenty years?" George Whitesides , *Angew. Chem. Int. Ed. Engl.* 29, 1209(1990)

Table 1. The "pull" of societal concerns and the "push" of basic research set the direction of chemistry.

Pull	Push
National Security	*Materials Chemistry*
Economic competition as the equivalent of war	Polymers
	Surfaces and interfaces
	Functional and "smart" materials
Health Care	Materials for manufacturing
An aging population	Environmentally compatible materials
Global epidemics	
Cost containment	*Biological Chemistry*
Drugs	Molecular recognition
	Evolution and self-assembly
The Environment	Bioenergetics
Global change	
Waste management	*Computational Chemistry*
Toxicology	Increasing power
	New architectures: massively parallel machines and neural nets
Energy	
Alternatives to fossil fuels	
Electricity	*Small Basic Science*
	Exploring the limits: very small; very fast; very large
Globalization	

Every science
Begins as philosophy and
ends as art.

-Will Durant-

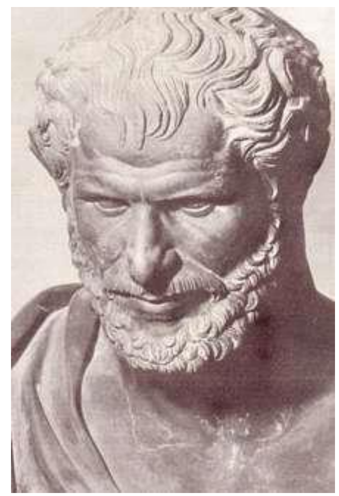
What is Science?

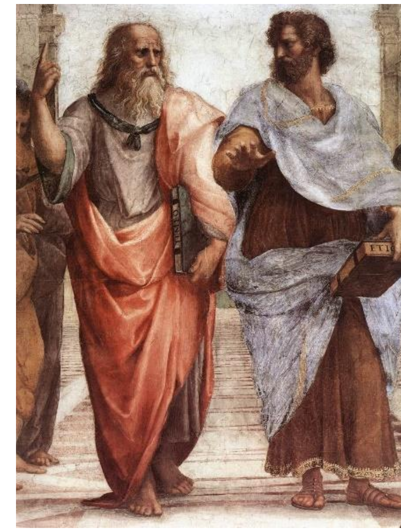
Old Greek: Natural Philosophy

Thalēs

Parmenides

Democritos





Platōn

Aristoteles

Nature에 대한 서양의 관점(고대그리스철학자들)

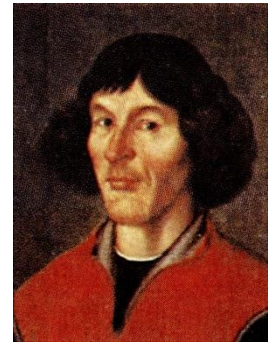
- Physical Objective

- We must know,
  We will know
  (Wir müssen wissen,
  Wir werden wissen)
  -David Hilbert-

- What ?

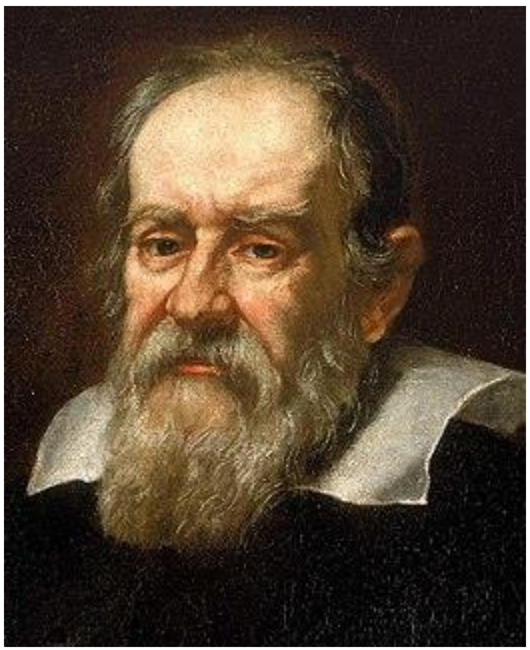
What is Science?

Modern: 16세기 이후(1543)

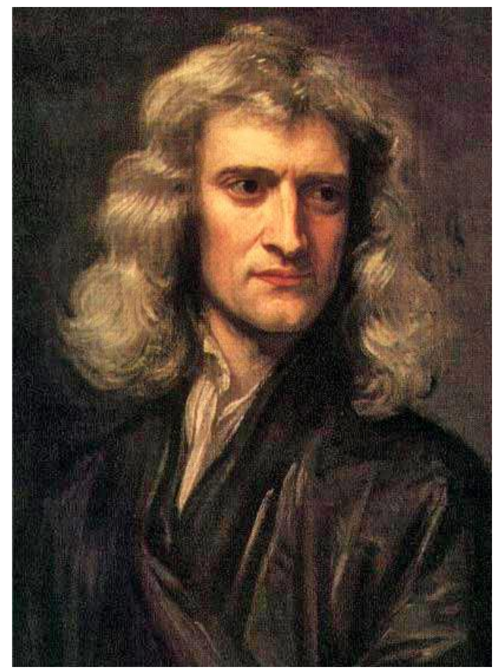


Copernicus

Vesalius



Galileo



Newton

Modern Science

- **Explain and (Re-)produce**
- **Mathematical Tool**
- **Not Why, but How**

What is Chemistry?
Origin: Alchemy

분자(유기, 무기) 반응에 의한 합성

- 화합물의 물성(물리적, 화학적)

- 화합물의 반응

엄청난 수의 분자들의 반응
1 mol ~ 10^{23} 분자

Explain : Physics, Physical Chemistry

(Re-)produce : Synthesis, etc.

Fundamental Thought in Physics & chemistry

"Phys & Chem advances on two feet :
The one is curiosity(Science),
another utility(Technology)."

Curiosity drives breakthrough on Utility

Theory → **Things**

1905

Fundamental Theory to explain Nature:

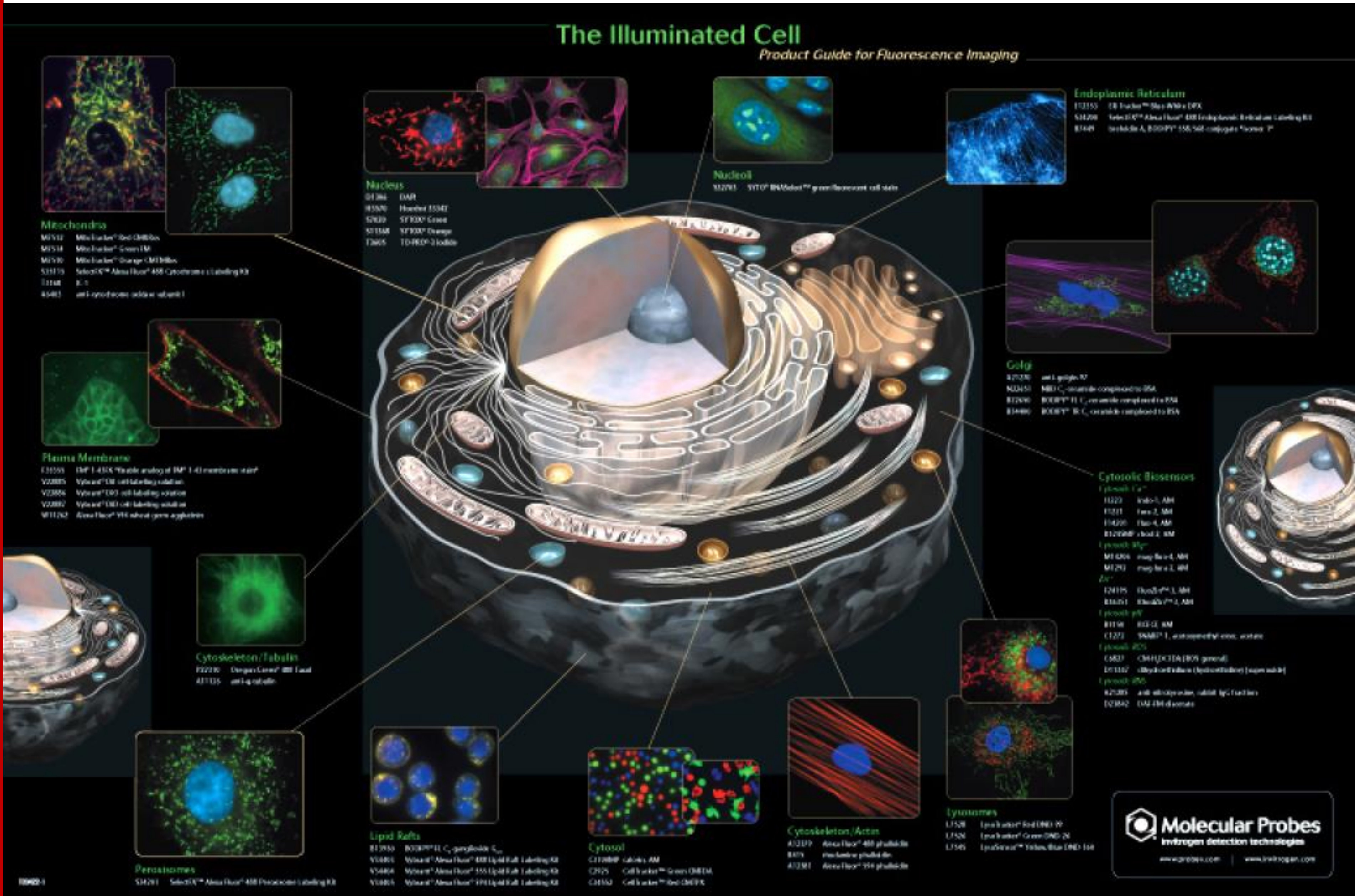
- Thermodynamic Laws (1st, 2nd, 3rd) → Statistics
- Elementary particles (Molecules, Atoms, Subatomic)
- 4 kinds of Force (Gravity, Electromagnetic, Strong, Weak)
- Quantum Mechanics (Classical Mechanics)

We need Other Fundamental theories?

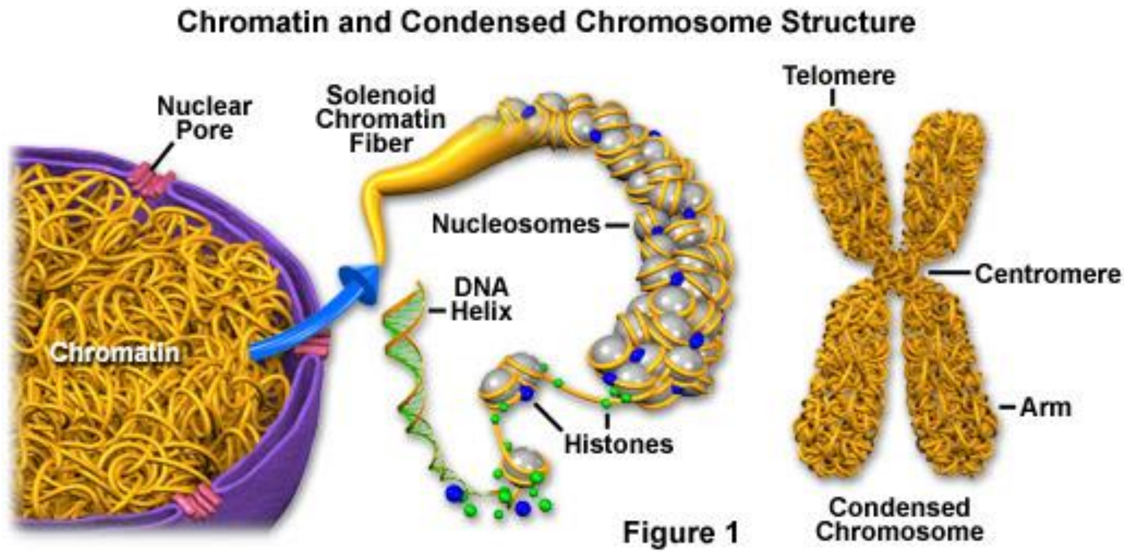
for What?, Maybe for life?

1905

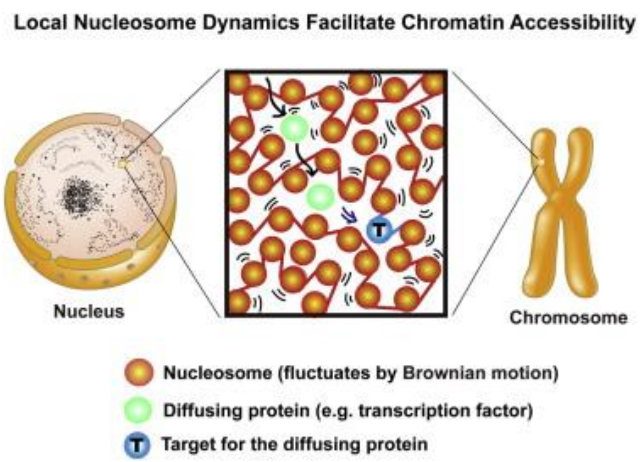
인체: 수십조개의 세포로 구성

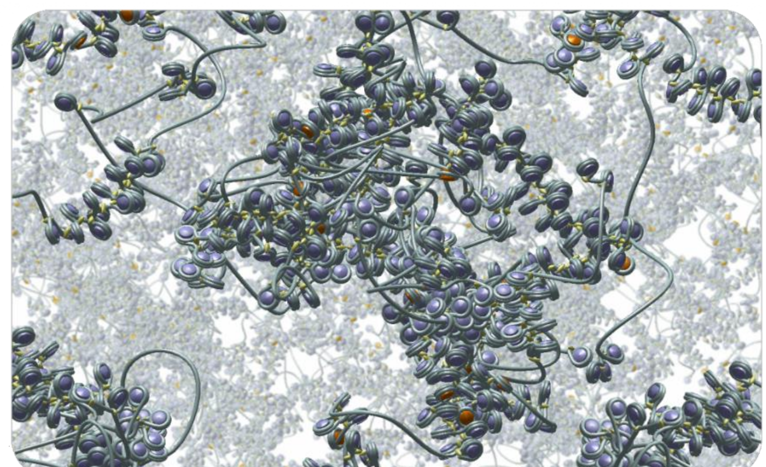


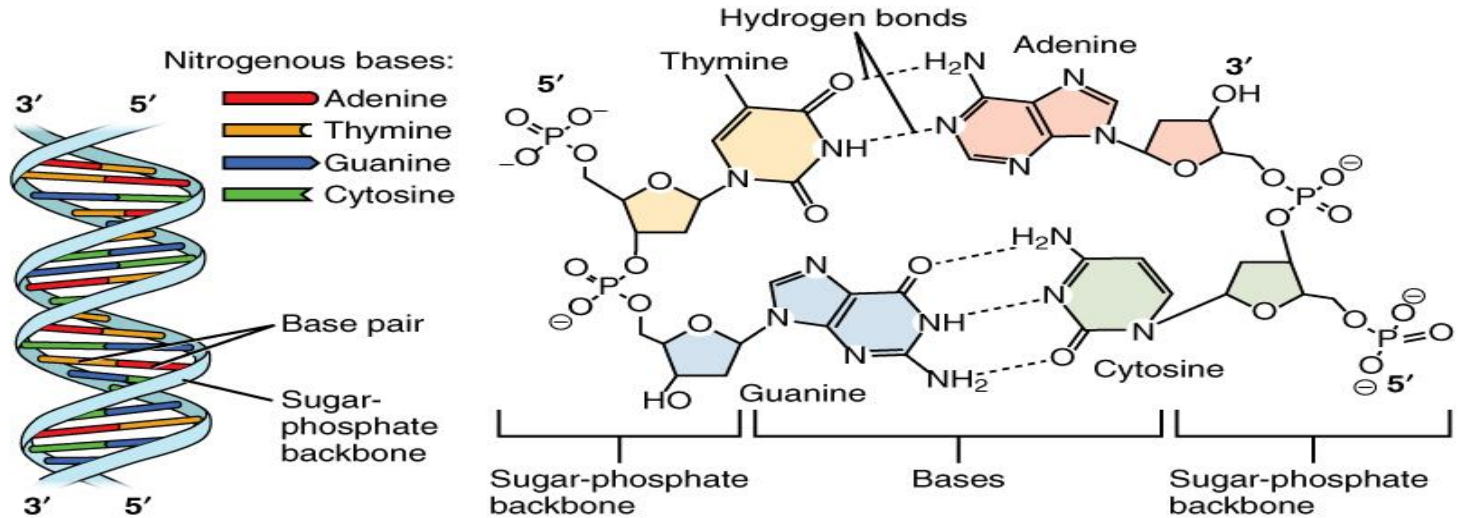
Chromosome & Chromatin



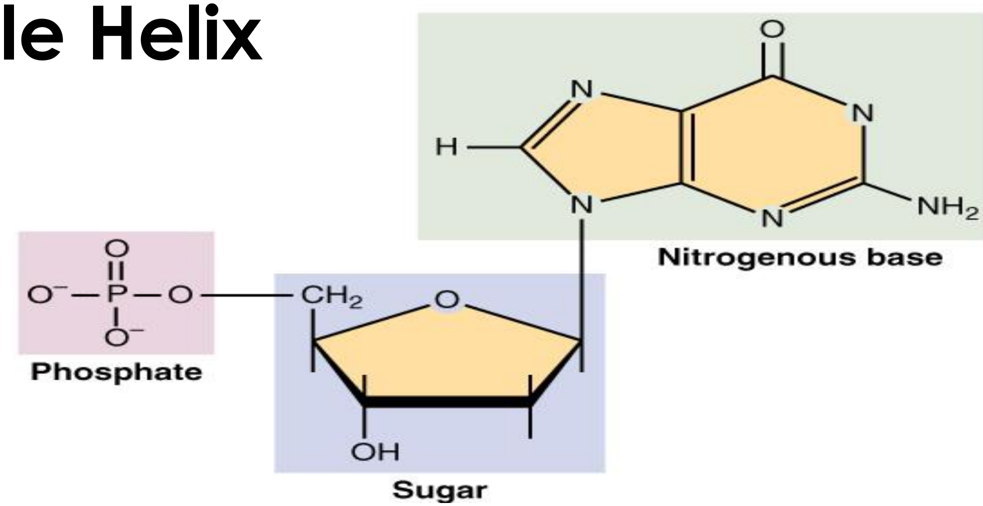
인간: 23쌍







Double Helix



Nucleotide

DNA(DeoxyriboNucleic Acid)

base사이 간격**-0.34nm,** 세포내 염기갯수**-30**억개 총 **2m**

RNA(RiboNucleic Acid)

Chemistry ⟷ Bio & Med Science(Life)

Low Level	High Level
Microscopic View	**Macroscopic View**
-Molecular science -Theory: Quantum Chemistry -Experiment: Spectroscopy etc. -Statistical Treatments	-Thermodynamics -Statistical Thermodynamics -Thermodynamics Function (T, P, V, etc)

Ultimate Goal of Bio & Med Science : What is life?

Life - Macroscopic phenomena, not molecular level

(dead of molecules ?)

We need its appropriate level description

1905

Mesoscopic scale description

There is no rigid definition for *mesoscopic physics*, but the systems studied are normally in the range of 100 nm (the size of a typical virus) to 1000 nm (the size of a typical bacterium). (By Wikiphedia)

But Condensed Matter Physics ,

especially related with Nanofablication & Nanotechnology

(Quantum Confinement effect, Interference effect, Charging effect, etc.)

not Bio & Med Science

Mesoscopic scale description

Atoms, Molecules : Quantum Mechanics
and/or Classical Mechanics

분자 사이의 상호작용 – 수학적으로 복잡

고전역학 : **Newton's 2nd law of motion**
양자역학 : **Schrödinger Equation**

among 4 kinds of forces : Electromagnetic

1905

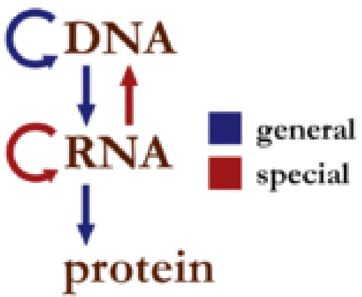
Bulk : Thermodynamics,

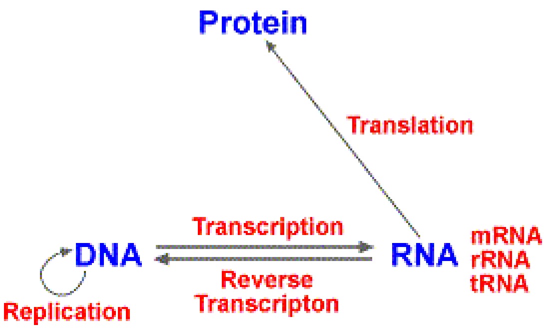
분자들의 모임 - Statistical thermodynamics

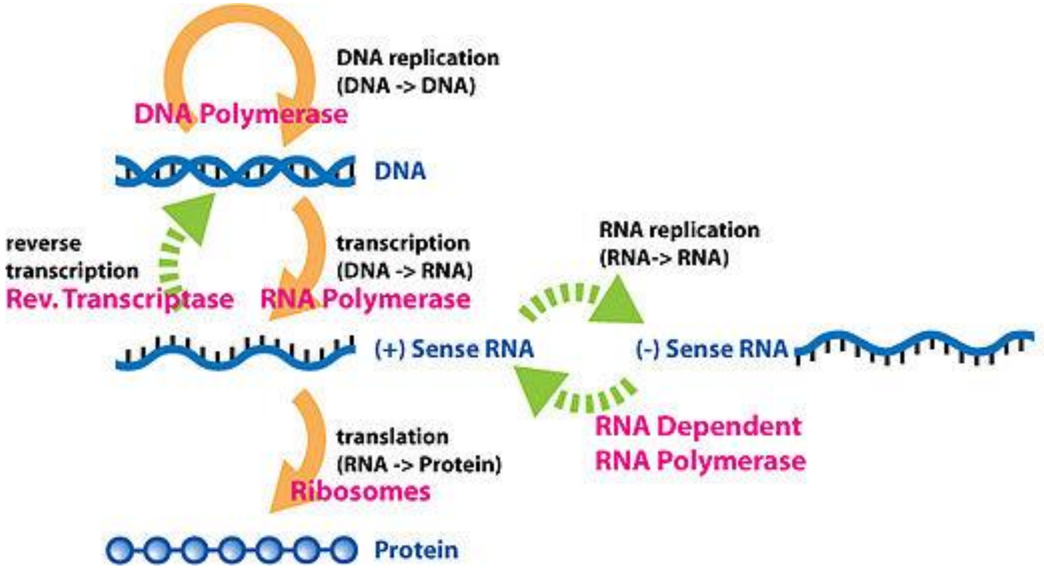
Random - Probability, Statistics

Can we accept everything of life only with QM, EM force, Random motion ?

생명의 원리 - Central Dogma (Francis Creek, 1958)

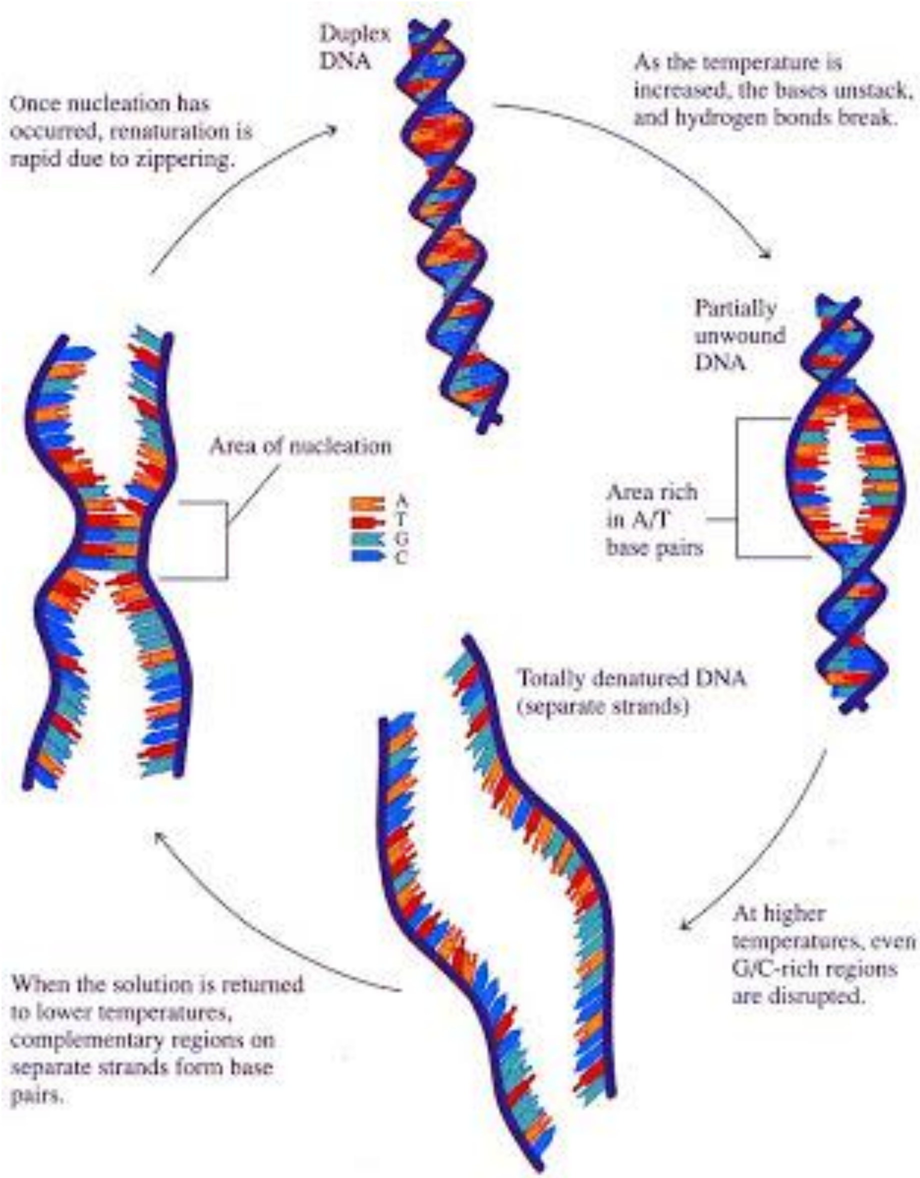




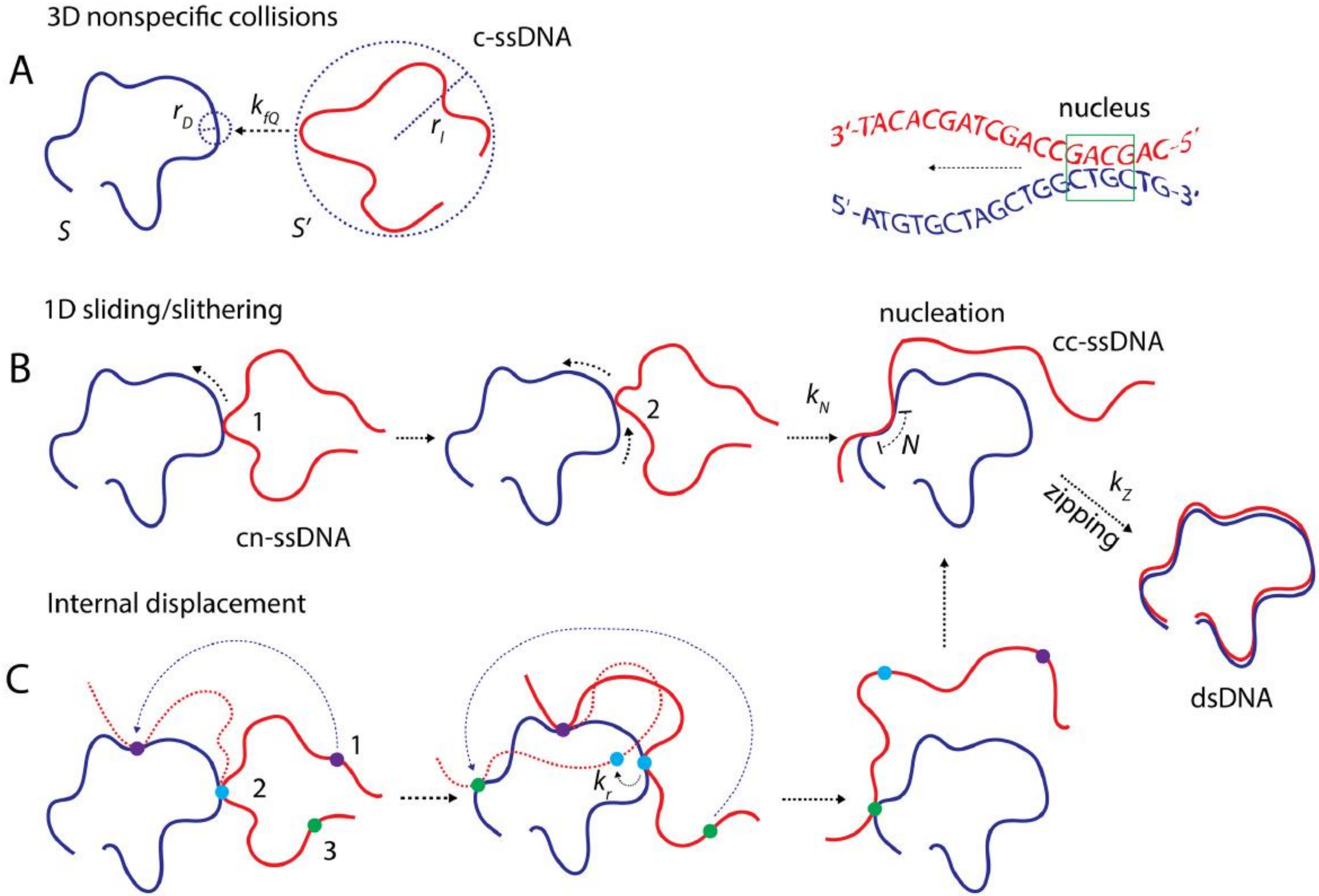


DNA

Denaturation
&
Renaturation



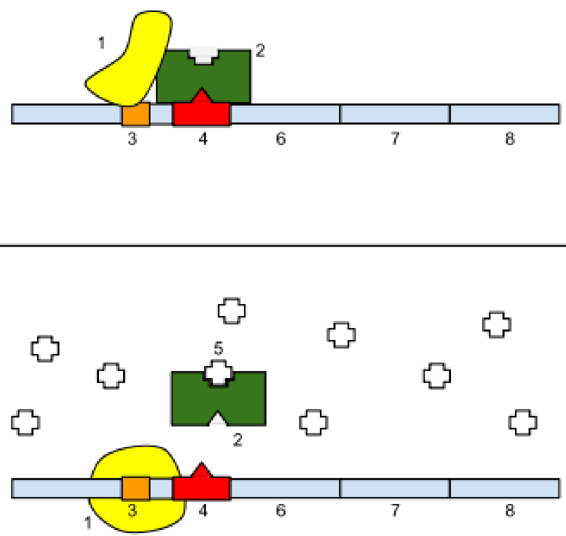
Mechanism of DNA Renaturation



Jacob and Monod model of transcriptional regulation of the *lac* operon by *lac* repressor(1961)
When *lac* repressor binds to a DNA sequence called the operator (O), which lies just upstream of the *lacZ* gene, transcription of the operon by RNA polymerase is blocked. Binding of lactose to the repressor causes a conformational change in the repressor, so that it no longer binds to the operator. RNA polymerase then is free to bind to the promoter (P) and initiate transcription of the *lac* genes; the resulting polycistronic mRNA is translated into the encoded proteins.
[Adapted from A. J. F. Griffiths et al., 1993, *An Introduction to Genetic Analysis,*5th ed., W. H. Freeman and Co.]

1965 Nobel prize(Physiology or Medicine)

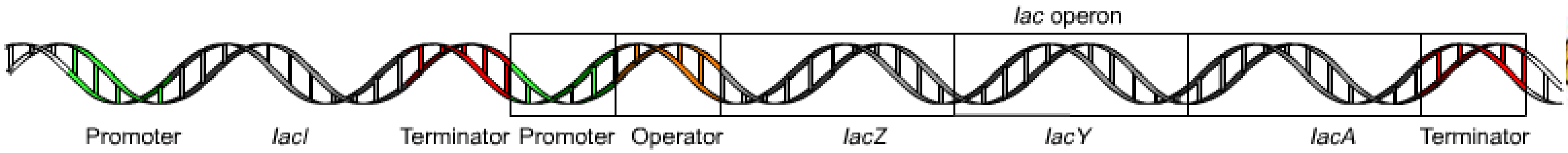
Lactase 합성



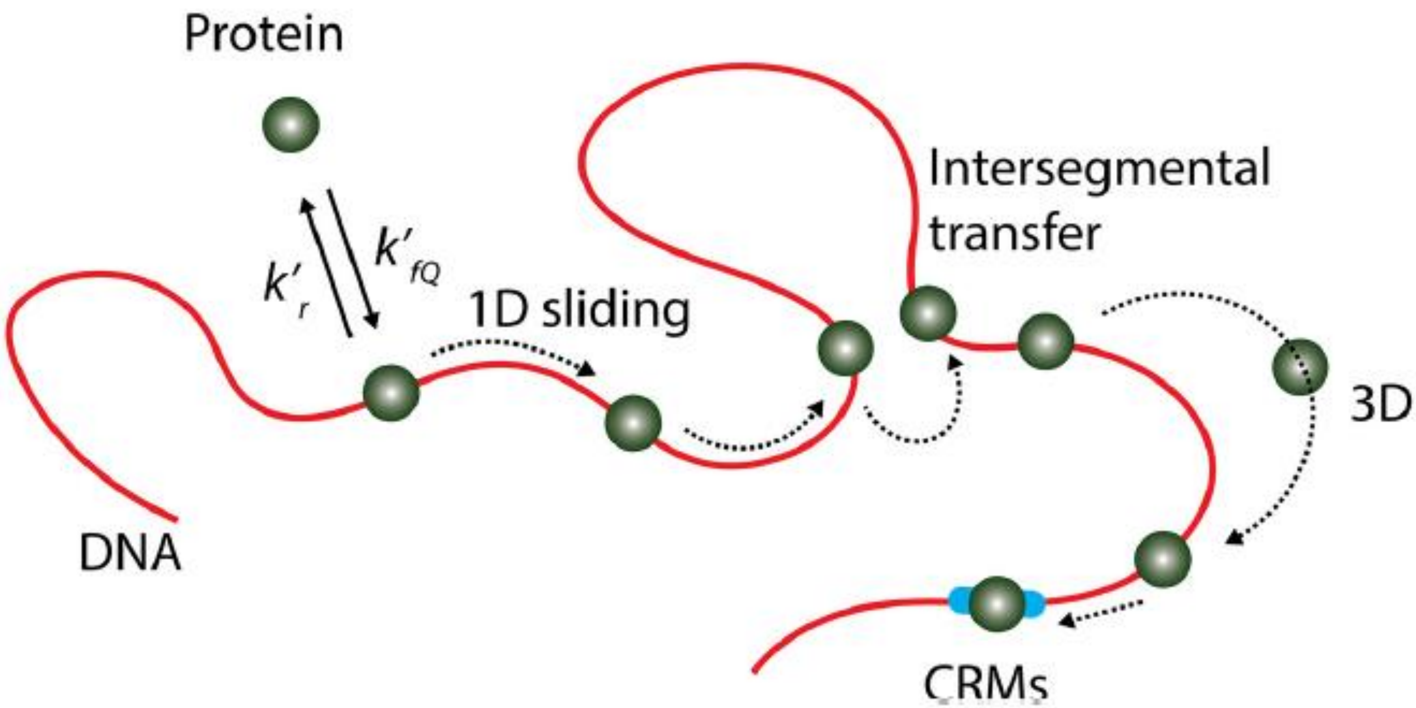
Operator site : 10-20 base pairs long

Top: The gene is essentially turned off. There is no lactose to inhibit the repressor, so the repressor binds to the operator, which obstructs the RNA polymerase from binding to the promoter and making lactase.
Bottom: The gene is turned on. Lactose is inhibiting the repressor, allowing the RNA polymerase to bind with the promoter, and express the genes, which synthesize lactase. Eventually, the lactase will digest all of the lactose, until there is none to bind to the repressor. The repressor will then bind to the operator, stopping the manufacture of lactase.

1: RNA Polymerase, 2: Repressor, 3: Promoter,4: Operator, 5: Lactose, 6: lacZ, 7: lacY, 8: lacA.



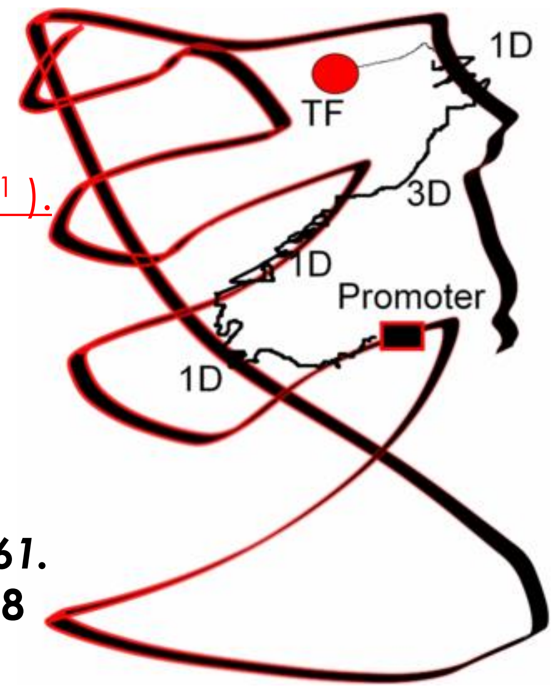
Site-specific DNA-protein interactions



Facilitated diffusion (Theory & Exp.)

An experimental measurement of the association rate between LacI and its operator sites provided a value of around 10^{10} M^{-1} s^{-1},
2-3 orders of magnitude higher than the diffusion limit(10^{8} M^{-1} s^{-1}).
(from **Smoluchowski equation & 최신 data)**

Riggs, A.; Bourgeois, S.; Cohn, M. *J. Mol. Biol. 1970, 53, 401*.
Halford, S. E.; Marko, J. F. *Nucleic Acids Res. 2004, 32, 3040*.



The hypothesis of facilitated diffusion of LacI along DNA is supported by both theoretical and experimental analyses.
-Winter, R. B.; Berg, O. G.; von Hippel, P. H. *Biochem 1981,20, 6961*.
-von Hippel, P.H. and Berg, O.G. J. Biol. Chem. 1989 264, 675–678

Facilitated Target Location

both 1D sliding and 3D Space hopping and jumping
(intramolecular dissociation/reassociation events)

Adam, G. & Delbrück, M. Reduction of dimensionality in biological diffusion processes. in Structural Chemistry and Molecular Biology (eds. Rich, A. & Davidson, N.) 198–215 (W.H. Freeman and Company, San Francisco; London, 1968)

1905

Facilitated diffusion (Theory & Exp.)

Real –time Single Molecule observation(resolution diffraction limit)
Xie group (Science 316, 1191(2007))

1D diffusion constant : $D_{1D} \sim 0.046\ \mu m^2\ s^{-1}$
3D diffusion constant : $D_{3D} \sim 3\ \mu m^2\ s^{-1}$

Apparent diffusion constant : D_{eff} ~0.40 $\mu m^2\ s^{-1}$

$$D_{eff} = D_{3D}(1 - F) + FD_{1D}/3$$ ***(F: fraction of time for nonspecific binding)***

$F \sim 90\%$

즉 **non-specsific binding** 후 **1D sliding search** 자리를 못 찾으면 다시 **dissociation**하면서 **3D search**를 통하여 다른 곳에 **non-specific binding** 과정을 반복하여 결국 자리를 찾아 **specific binding.**

지지 연구: **"What matters for lac repressor search in vivo-sliding, hopping, intersegment transfer, crowding on DNA or recognition?" Berg and Elf Nucleic Acid R 43 3454(2015)** 등등

반론 연구 : **"RNA polymerase approaches its promoter without long-range sliding along DNA" L. J. Friedmann PNAS 110, 9740 (2013)** 등등

Searching a rare event : Global minimum of binding energy?

Table 1 Copy numbers in *Escherichia coli*

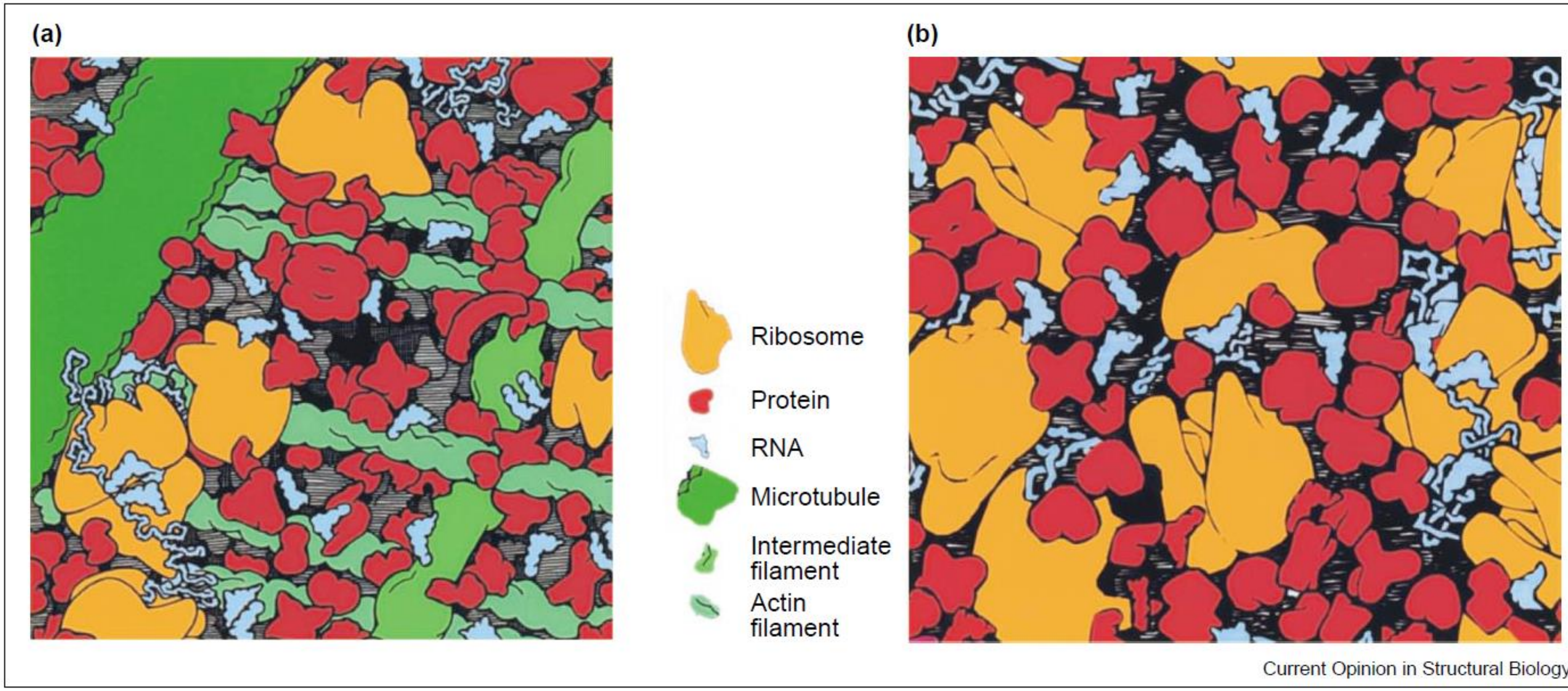
Molecular unit	Number	Reference(s)
Replication errors per genome	0.002	(23)
Double-strand breaks per genome	0.2	(66)
Replication forks per cell	1.5–6	(12)
Gene copies per cell	1–5	(12)
β-galactosidase tetramers per uninduced cell	1	(15)
F-plasmids per cell	1–3	(30)
Transposon copies per genome	1–15	(10)
lac repressor tetramers per cell	5	(33)
RNAPs per induced *lac* gene	5–20	(44)
DNA polymerase III per cell	10–20	(13)
lacZ mRNA per cell	10–30	(44)
Ribosomes per *lac* mRNA	20	(44)
DnaG primases per cell	50	(68)
Actively transcribing RNAPs per cell	200–2000	(12)
RecA molecules per cell	1000	(43)
Single-stranded DNA binding protein	1000–7000	(11, 75)
Total RNAPs per cell	1000–10,000	(12)
Ribosomes per cell	7000–50,000	(12)
β-galactosidase tetramers per induced cell	10,000	(44)
Total nucleoid proteins (e.g., Fis, HU, H-NS) per cell	50,000–200,000	(4)
tRNA per cell	60,000–400,000	(12)

Targeting sites on DNA : a targeting site among 10^6 – 10^9 decoy sites on a long DNA molecule

Crowding in a cell

Eukaryotic

Prokaryotic



The crowded state of the cytoplasm in **(a)** eukaryotic and **(b)** *E. coli* cells. Each square illustrates the face of a cube of cytoplasm with an edge 100 nm in length. The sizes, shapes and numbers of macromolecules are approximately correct. Small molecules are not shown. Adapted with permission from [21].

Concentration of Macromolecules : 50-400g/L

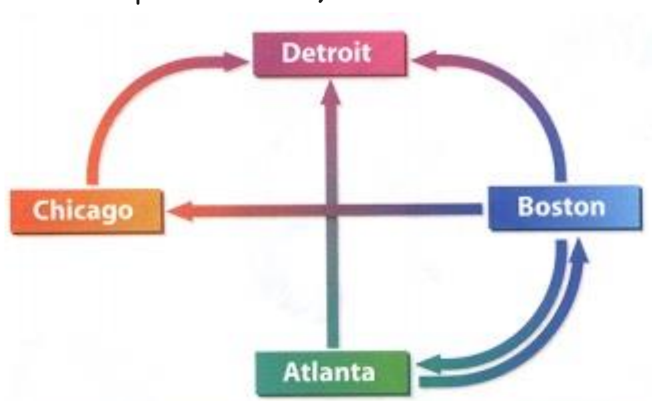
정확한 과학적 이해가 안되어도 활용 가능?

DNA Computing

Adleman, L. M. (*Science*. **266,** 5187, 1994).
"Molecular computation of solutions to combinatorial problems".

“traveling salesman” problem

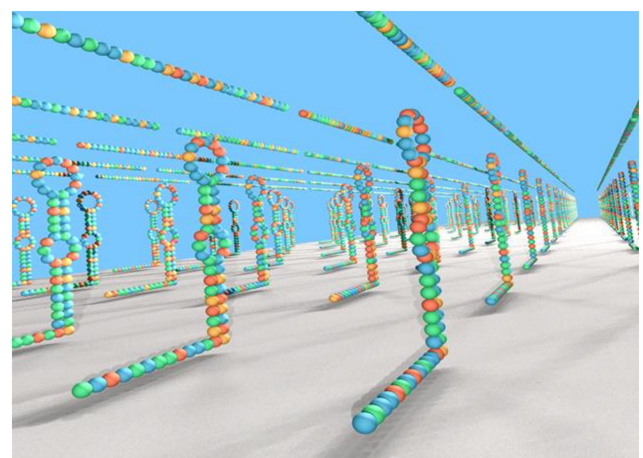
(P–NP problem)



CITY	DNA NAME	COMPLEMENT
ATLANTA	ACTTGCAG	TGAACGTC
BOSTON	TCGGACTG	AGCCTGAC
CHICAGO	GGCTATGT	CCGATACA
DETROIT	CCGAGCAA	GGCTCGTT

FLIGHT	DNA FLIGHT NUMBER
ATLANTA - BOSTON	GCAGTCGG
ATLANTA - DETROIT	GCAGCCGA
BOSTON - CHICAGO	ACTGGGCT
BOSTON - DETROIT	ACTGCCGA
BOSTON - ATLANTA	ACTGACTT
CHICAGO - DETROIT	ATGTCCGA

A DNA computer can solve extremely difficult math problems.



Fundamental Theory :

- Thermodynamic Laws (1st, 2nd, 3rd) → Statistics
- Elementary particles : Molecules, Atoms
- Force : Electromagnetic
- Quantum Mechanics (and/or Classical Mechanics)

Those are enough to explain life?

1905

생명현상에서 고려해야 할 것들

- 소수의 매우 큰 분자들**(**단백질, 핵산 등**)**사이의 반응
  (더군다나 세포내의 **Macromolecular crowding)**

- **-** 생명의 방향성 **:** 분자들의 무작위 운동으로 설명 가능할까**?**

Schrödinger : Negative Entropy?

1905

생명현상에서 고려해야 할 것 들

- 소수의 매우 큰 분자들(단백질, 핵산 등)사이의 반응

상호작용의 표현 – Potential(Central) : Electromagnetic pair potential & attraction(long)/repulsion(short)

New potential function? :
Casimir force,
Krugman potential(?)
etc.

New "action at a distance"? :
Spooky action at a distance(by Einstein)

1905

Krugman potential

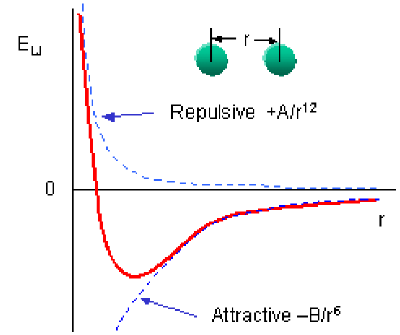
Paul Klugman : The self-organizing Economy(1996)

J Bates Clark medal 1991, Nobel Prize Economics 2008

Peddling Prosperity (95) Pop Internationalism(96) etc.

Inverse Potential :

일반적 pair potential, long attraction-short repulsion



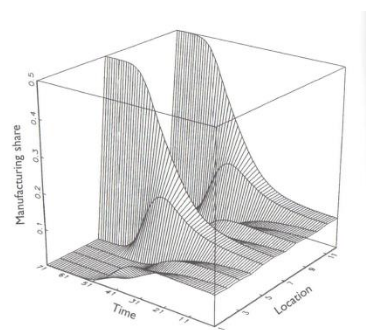
Krugman: Urban morphogenesis – Edge city model

- **potential: multi interaction, short attraction-long repulsion**
- **one dimensional cyclic boundary condition**

Locations of market potential:

$$P(x) = \int (Ae^{-aR_{xz}} - B\,e^{-bR_{xz}})\lambda(z)dz$$

$$\frac{a}{b} > \frac{A}{B} > \frac{b}{a}$$



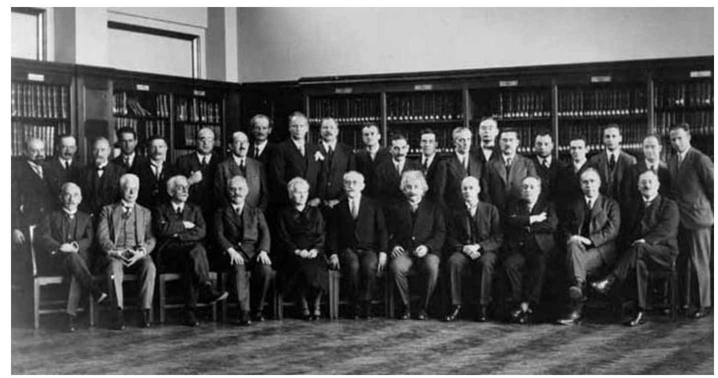
x: location of firms
R_{xz} : distance between x and z
A: centripetal (attr) B: centrifugal(repel)
a > b 때문에 agglomeration 생김
λ(z) : density of firms

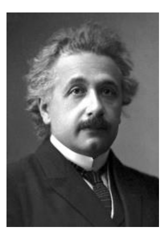
Quantum Mecheanics : very weird !!!

- Probability: wavefunction 의미
- Superposition: Schrödinger's cat
- Uncertainty principle: Entanglement

5th Solvay conf(1927)

6th Solvay conf(1930)



VS


Hidden Variable

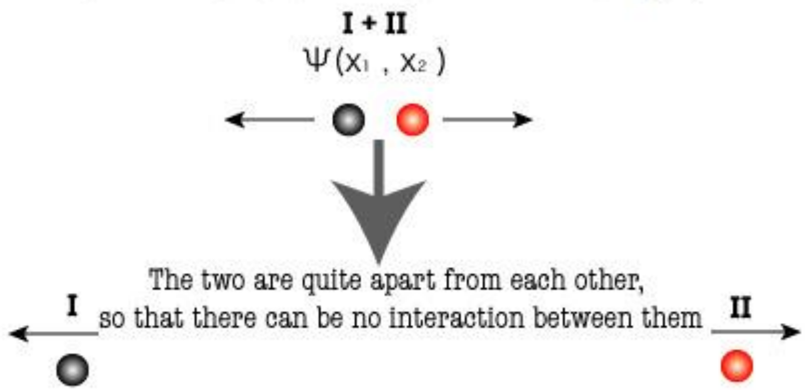
Copenhagen

1905

Quantum Mechanics:Einstein-Podolsky-Rosen(EPR) paradox

Can Quantum-Mechanical Description of Physical Reality Be Considered Complete?
Phys. Rev. 47, 777–780 (1935)

EINSTEIN-PODOLSKY-ROSEN PARADOX, (1)

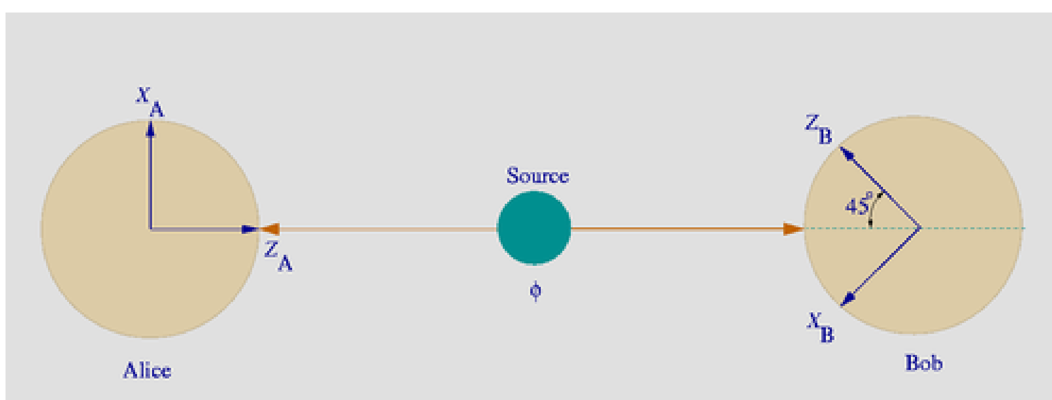


Suppose you measure the momentum of the black particle (I); then you can know the momentum of the red particle (II) as well. Likewise, if you measure the position of the black, then you can know the position of the red as well. In both cases, the measurement can be done **without disturbing** the red (since there can be **no interaction** between the black and the red).

Einstein called this the *'spooky-action-at-a-distance'*, which he could not accept due to the violation of 'principle of locality'.

QM : Hidden Variable

Bohm version (1950년대)



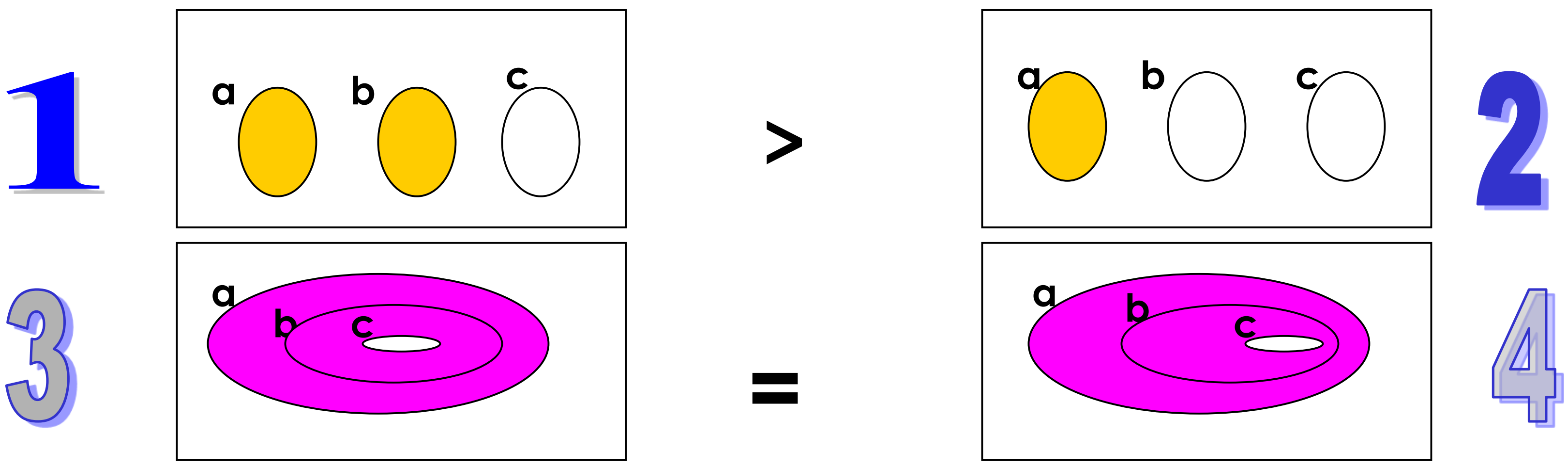
Quantum Entanglement

Measurements on spatially separated quantum systems can instantaneously influence one another.

1964 : Bell’s Inequality : QM(국소성 부정) vs HV(숨은변수) test 고안

Bell's Inequality Equation

$$N(a \cap \bar{b}) + N(b \cap \bar{c}) \geq N(a \cap \bar{c})$$



1905

Quantum ⟺ Classical

Non-Locality Locality

There exists a boundary size?

Then, molecules and organisms for life?

- 생명의 방향성 : 분자들의 무작위 운동으로 설명 가능할까?

Random motion : Stochastic
Brownian Ratchet?
Self Organized Criticality?

Probability : Negative Entropy(Schrödinger)
Shannon Entropy (Information entropy) ?
Baysian - Qbism

Quantum Biology : Quantum Mechanics for life

-Quantum Coherence:

Photosynthesis(Fleming)

-Quantum Tunneling:

Enzyme reaction(Klinman)
Smelling(Turin)
DNA mutation

-Quantum Entanglement

Magnetoreception by cryptochrome(Schulten)
(bird migration)

1905

Probability for life

확률의 4가지 의미

- 대칭성에 의한 수학적 확률
- 데이터에 의한 빈도의 확률 – **Frequentist**
- 인간의 심리.주관에 바탕을 둔 확률 – **Baysian**
- 증명 가능한 논리적 확률

Fundamental Thought in Physics & chemistry

Chemistry : 만들어내는 것

유기화학, 생물화학, 무기화학, 재료화학 등등

Physics : 생각하게 하는 것

이론 들 (양자역학 등등)

Basis for Breakthrough during 20th Century

Quantum Mechanics, Relativity

From Matters(Atoms, Light, Stars, etc.)

Basis for Breakthrough during 21th Century?

For Life

에사키 레오나(73물리학상)의 좋은 연구를 위한 필요조건

-지금까지 해온 것에 구애 받아서는 안된다.

-훌륭한 스승을 존경하는 것은 좋지만 빠져들어서는 안된다.

-무용한 것은 버리고 자신에게 도움이 되는 정보 만 취한다.

-때로는 싸움을 피해서는 안된다

-언제까지나 수수한 감성과 지적 호기심을 잃어서는 안된다.

有朋 自遠方來면 不亦樂乎아

친구가 먼 지방으로부터 찾아온다면
즐겁지 않겠는가

人不知而不慍이면 不亦君子乎아

사람들이 알아주지 않더라도 서운해 하지 않는다면
군자가 아니겠는가

- 論語(논어): 學而(학이)편-

I am a scientist?

爲己之學, 自得之味
(위기지학, 자득지미)

감사합니다