

# Advanced Nanotechnology (B)



- Class hour: every Friday, 09:30-12:10
- Classroom: P101, 1F, IoP

# Tentative Schedule

- 2/23 Introduction
- 3/1 Nuclear Acids, DNA, RNA, Sequencing
- 3/8 Amino Acids, Proteins, proteomic
- 3/15 Glycobiology and lipid
- 3/22 Synthesis and Characterization of NPs
- 3/29 NPs for diagnostic
- 4/12 NPs for Therapeutic
- 4/19 Imaging or other updated topic
- 4/26 Dr. Tung
- 5/3 Midterm

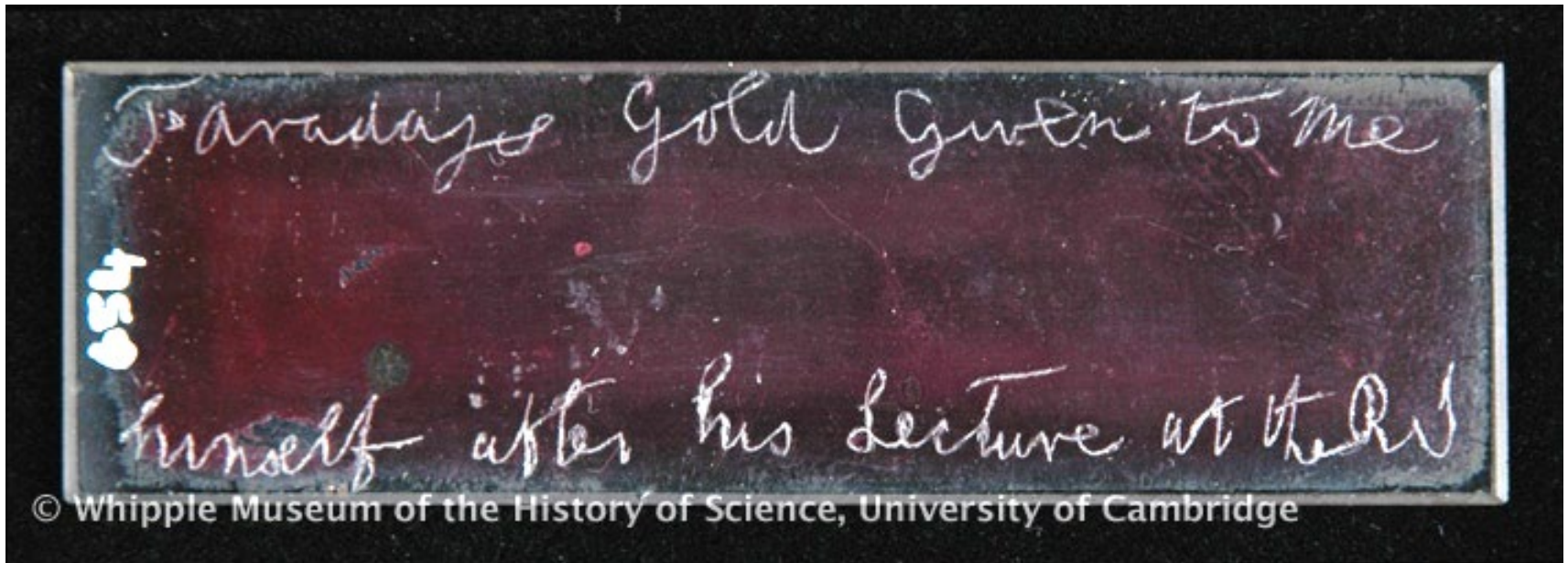
- Friday 9:30-12:10
- Midterm: 5/3 (60%, tentative)
- Final: 6/7 (Dr. Tung, 40%, tentative)
  
- Dr Tung: 4/26, 5/10, 5/17, 5/24, 5/31

# What is Nanotechnology?

- Nanotechnology is the science, engineering, and technology conducted at the nanoscale, which is about 1 to 100 nanometers.
- Significance: Manipulating matter on an atomic, molecular, and supramolecular scale for the fabrication of macro-scale products.
- Applications: medicine, electronics, biomaterials, energy production, and environmental protection



# Faraday's Gold Sol



1856  
20-40 nm gold

# What is nano?

## The Scale of Things – Nanometers and More

### Things Natural

Dust mite  
200  $\mu\text{m}$

Human hair  
 $\sim 60\text{-}120 \mu\text{m}$  wide

Ant  
 $\sim 5 \text{ mm}$

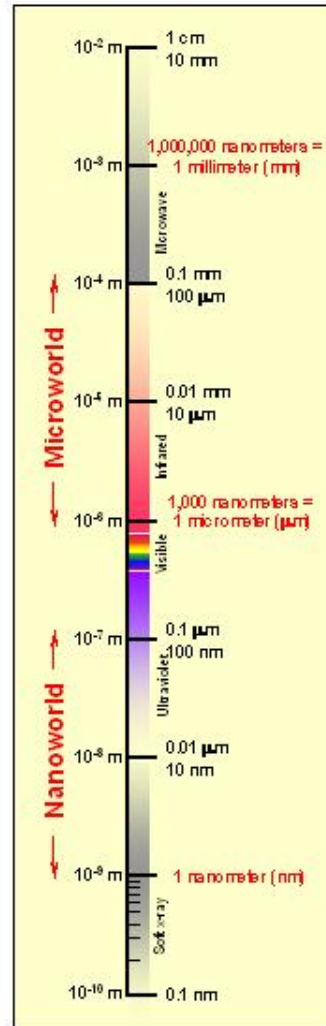
Fly ash  
 $\sim 10\text{-}20 \mu\text{m}$

Red blood cells with white cell  
 $\sim 2\text{-}5 \mu\text{m}$

ATP synthase  
 $\sim 10 \text{ nm}$  diameter

DNA  
 $\sim 2\text{-}12 \text{ nm}$  diameter

Atoms of silicon spacing  $\sim$  tenths of nm



### Things Manmade

Head of a pin  
1-2 mm

Micro Electro Mechanical (MEMS) devices  
10 - 100  $\mu\text{m}$  wide

Pollen grain

Red blood cells

Zone plate x-ray "lens"  
Outerring spacing  $\sim 35 \text{ nm}$

Self-assembled, Nature-inspired structure  
Many 10s of nm

Nanotube electrode

Quantum corral of 48 iron atoms on a copper surface  
positioned one at a time with an STM tip  
Conical diameter 14 nm

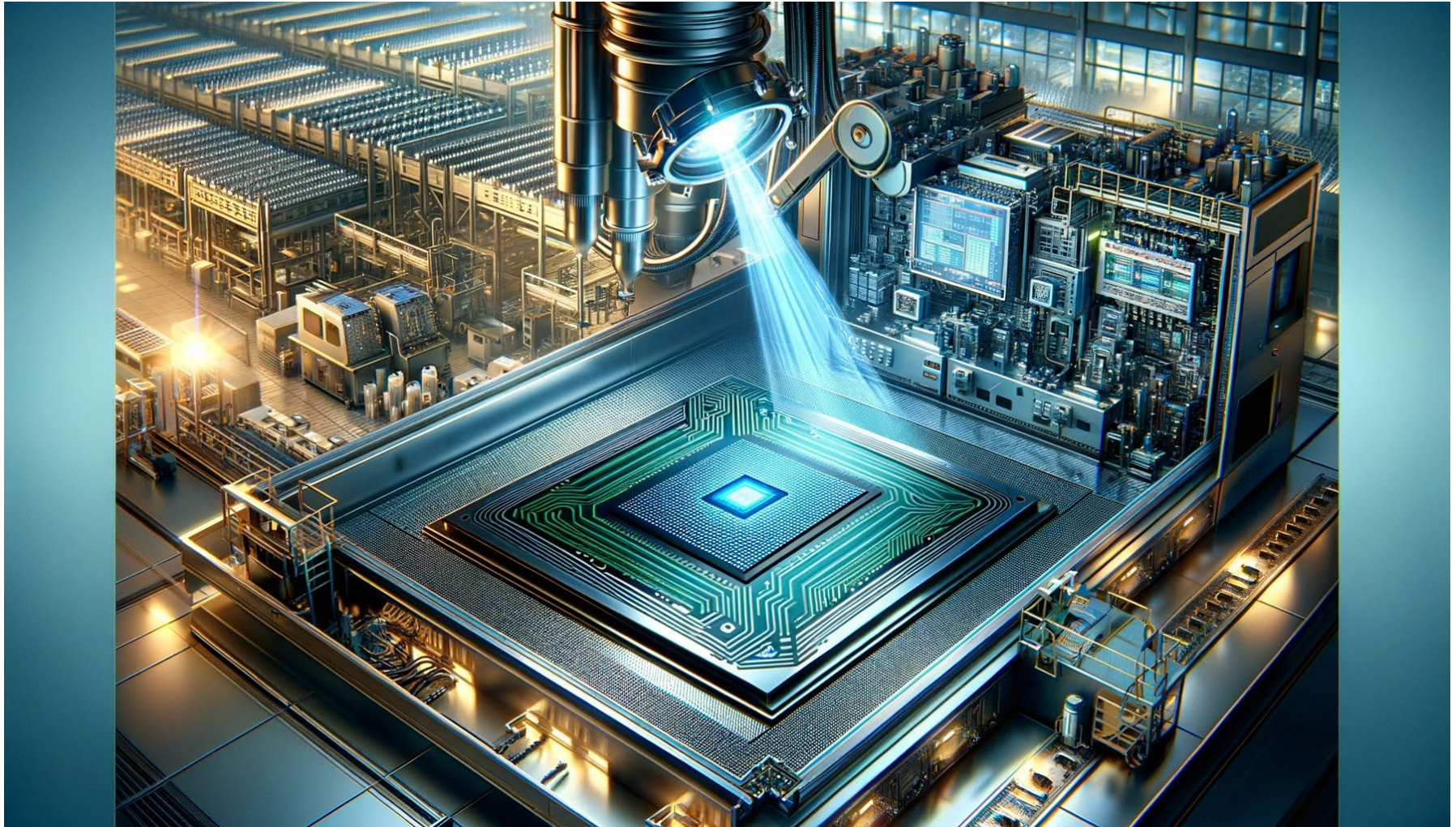
Carbon nanotube  
 $\sim 1.3 \text{ nm}$  diameter

Carbon buckyball  
 $\sim 1 \text{ nm}$  diameter

**The Challenge**

*Fabricate and combine nanoscale building blocks to make useful devices, e.g., a photosynthesis reaction center with integral semiconductor layer.*

# Chips fabricated by the Optical Lithography



# Lithography Roadmap

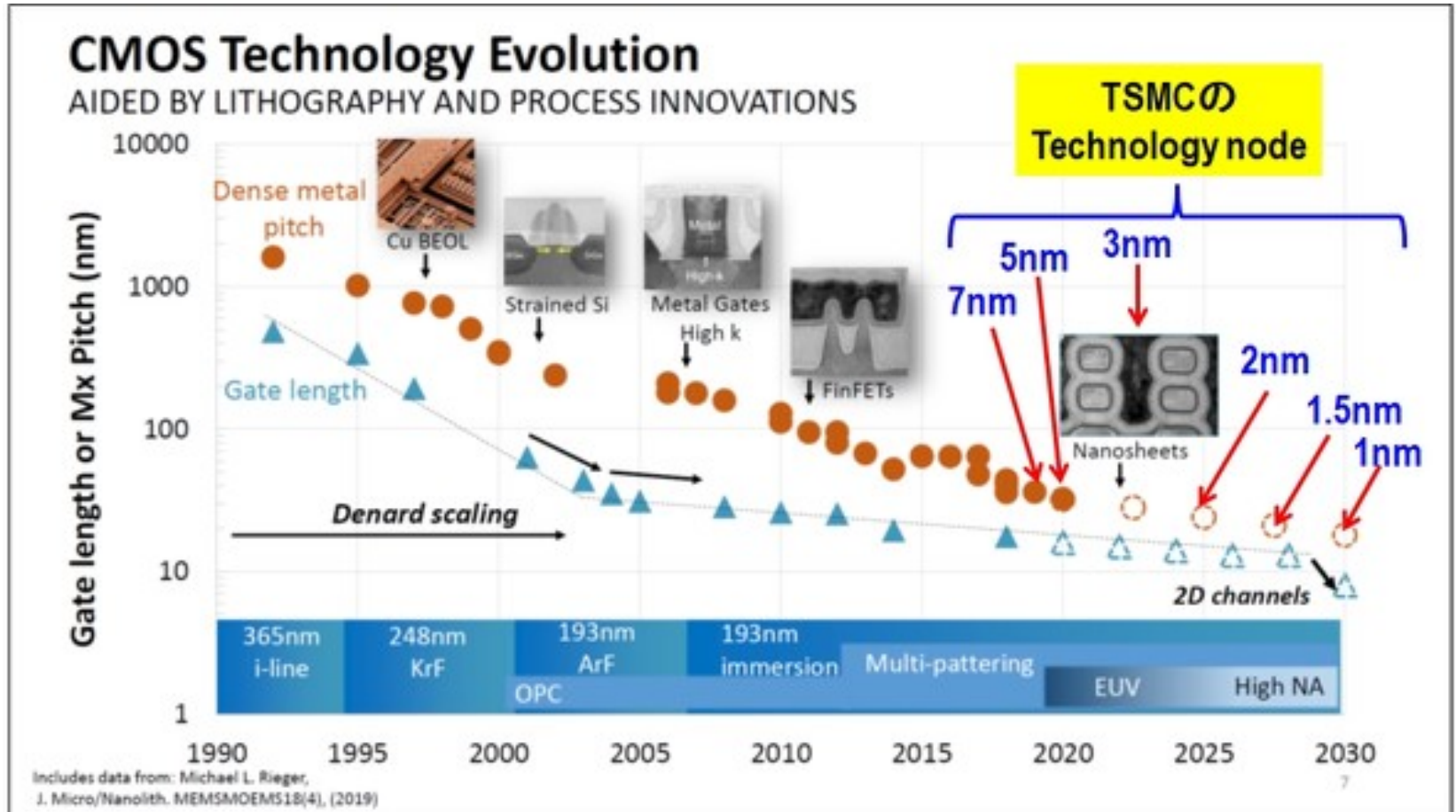


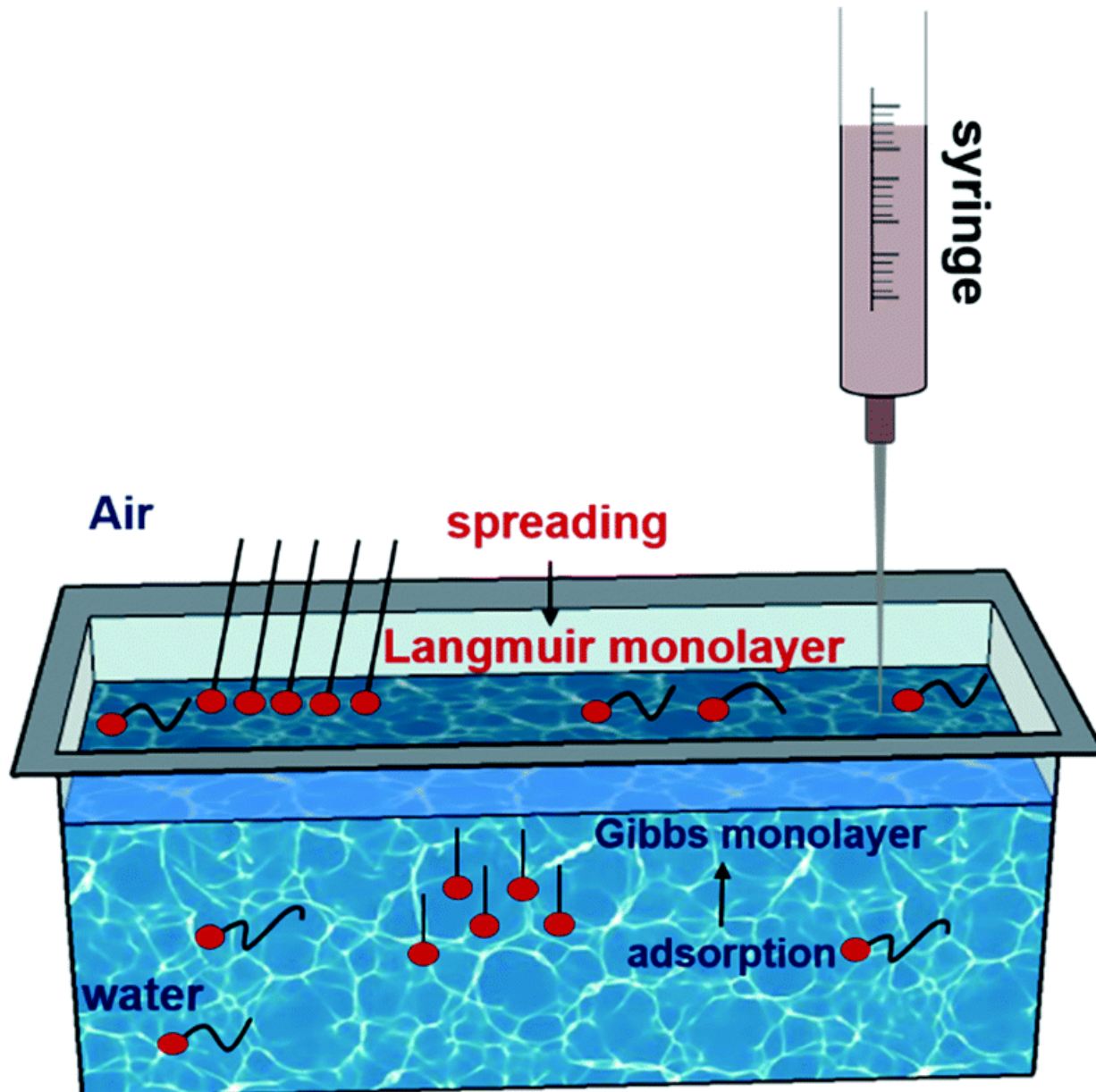
図5 ロジックのCMOS技術の進化



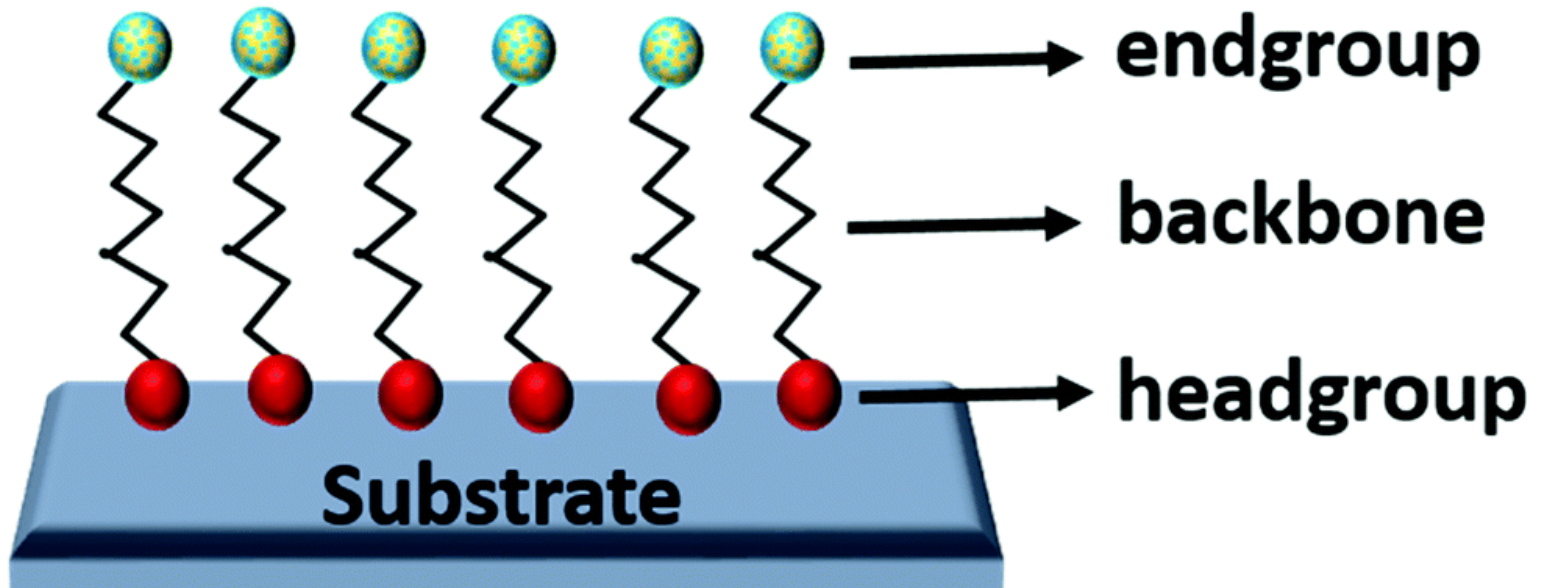
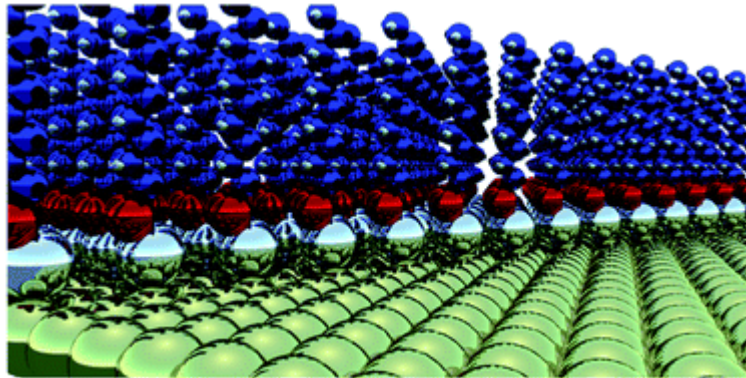
# Lithography Roadmap



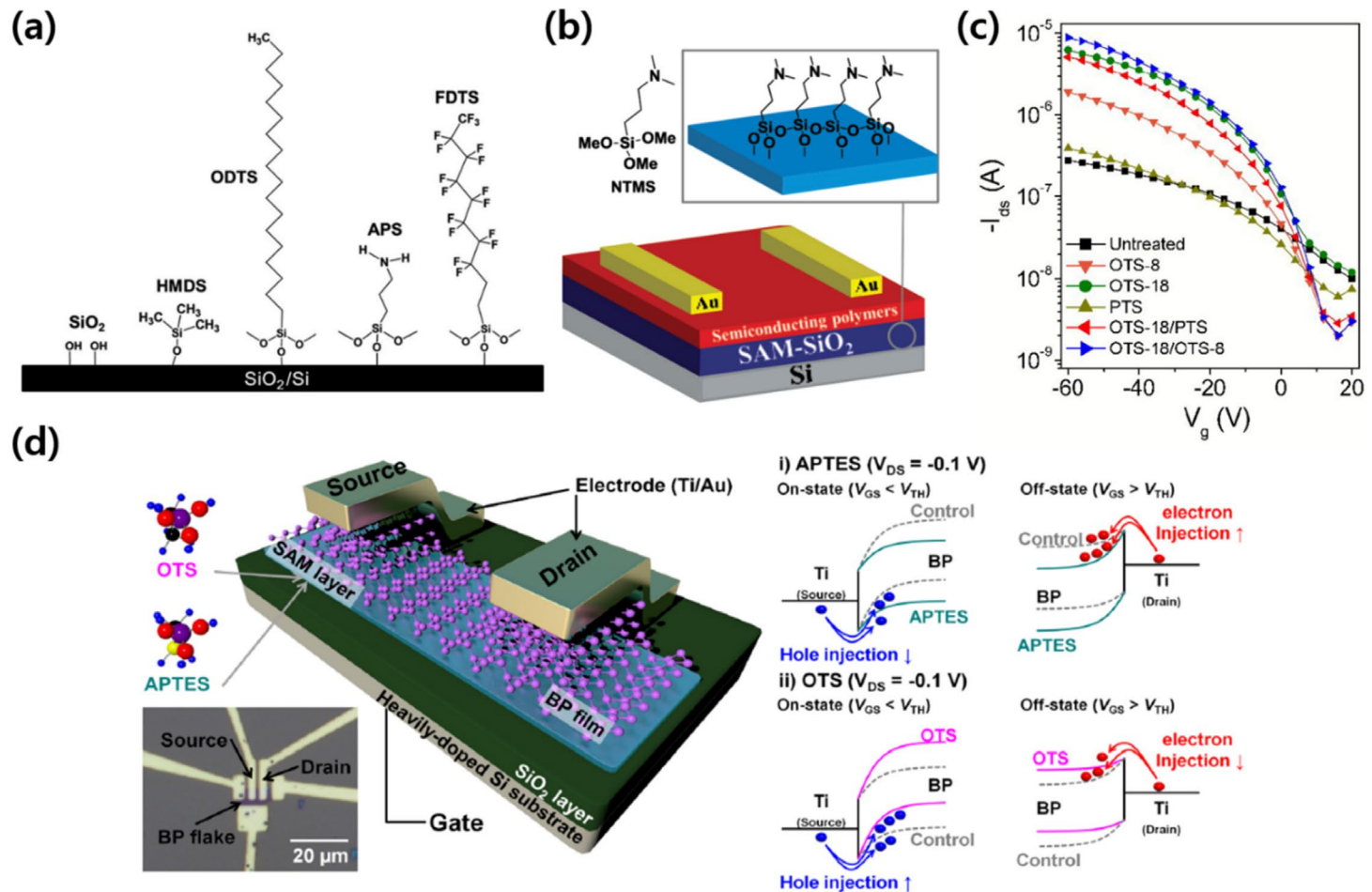
# Self-Assembly Monolayers



# Self-Assembly Monolayers



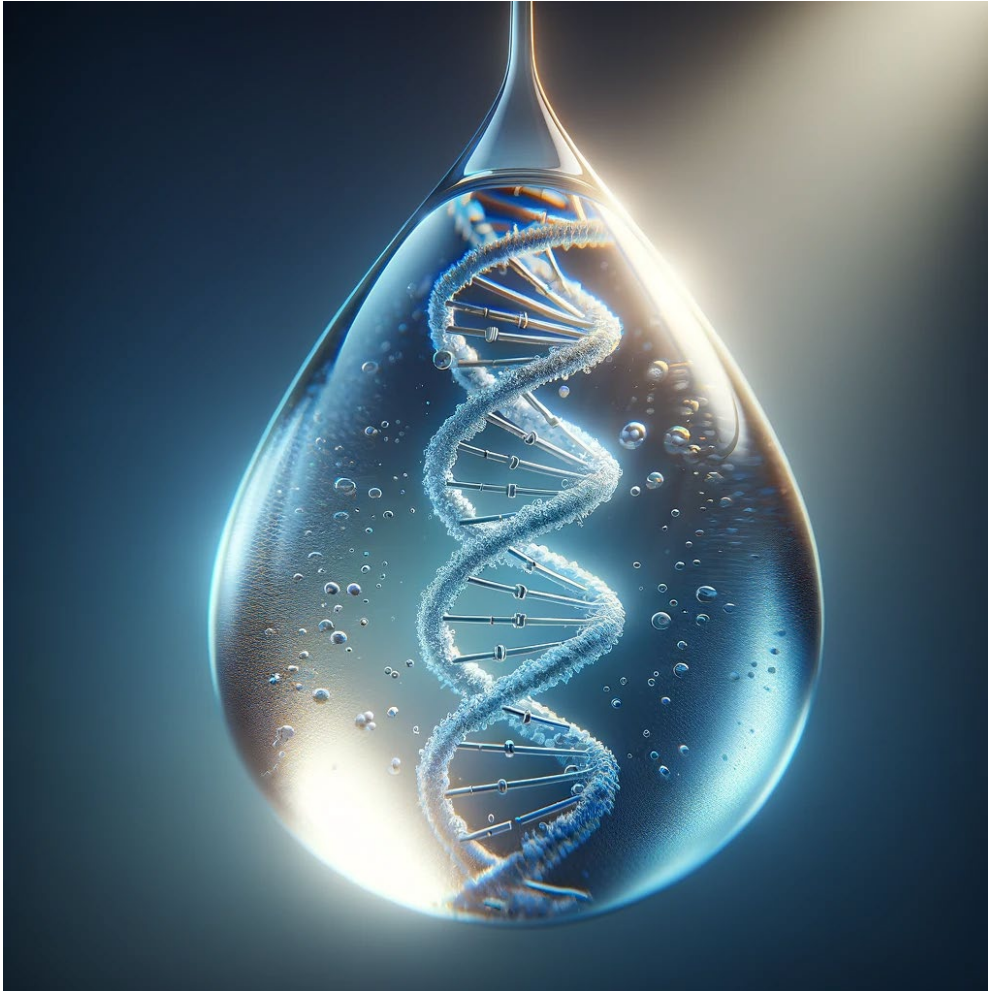
# Molecular Electronic



# A busy cellular factory



# One molecule in one drop of water



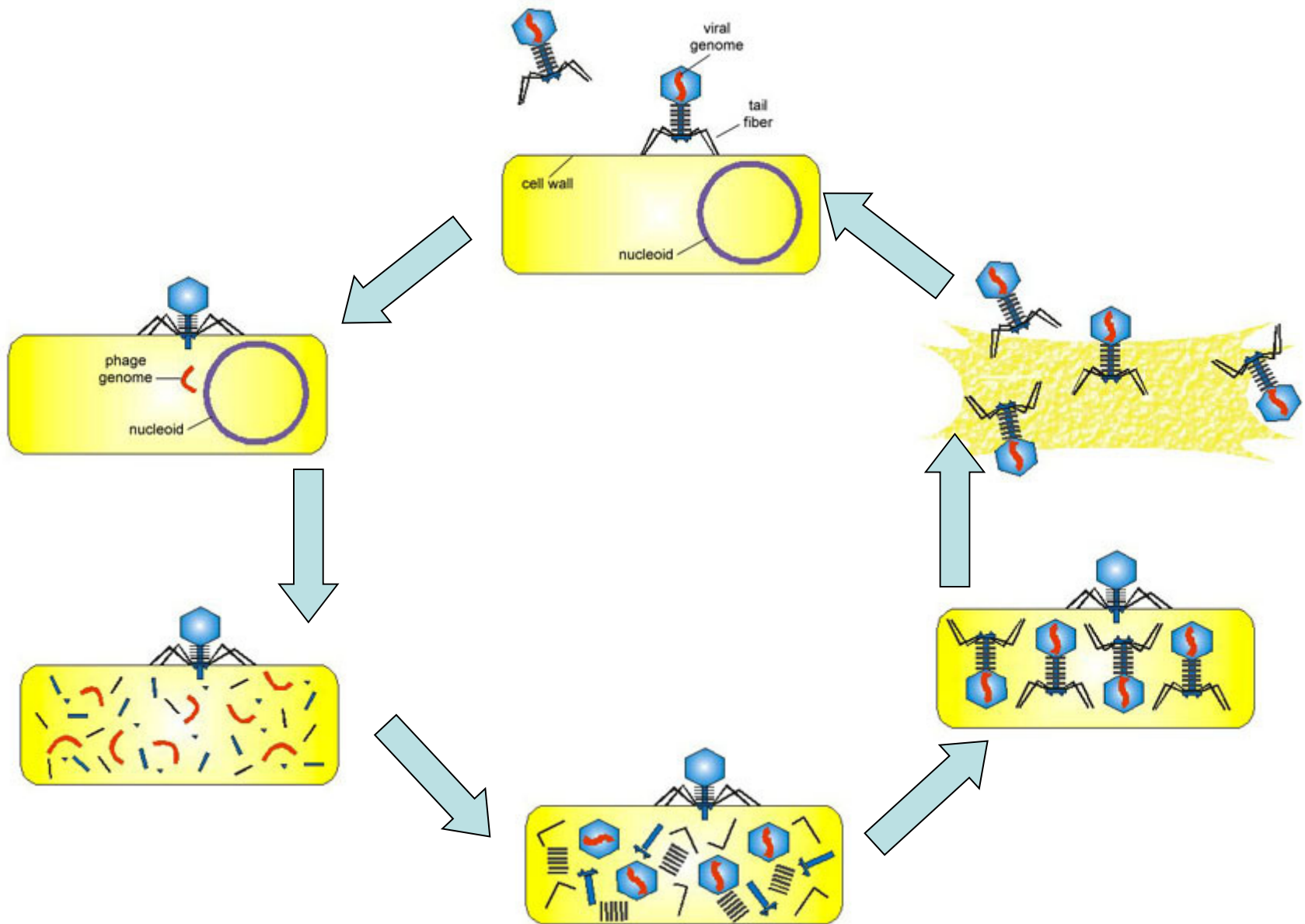
1 drop of water = 1/20 cc

$$1/(6 \times 10^{23}) / (1/20) = 3 \times 10^{-20} \text{ M}$$

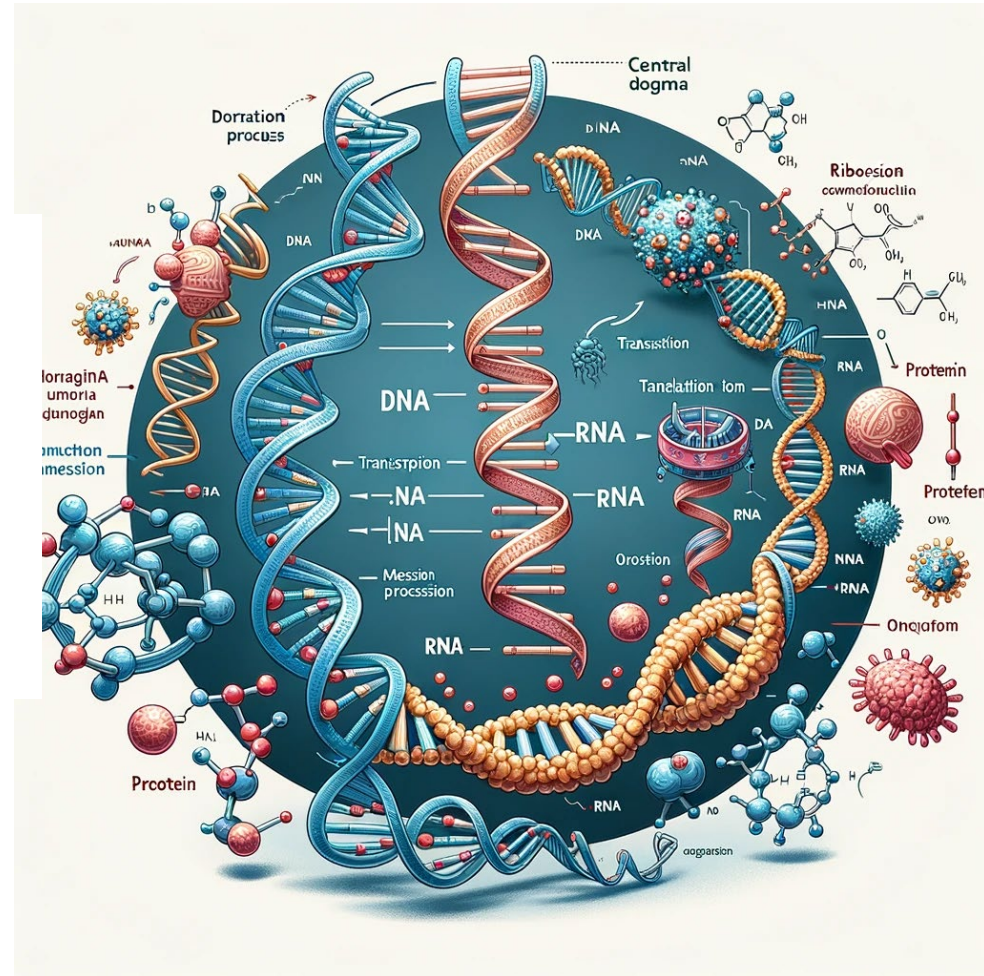
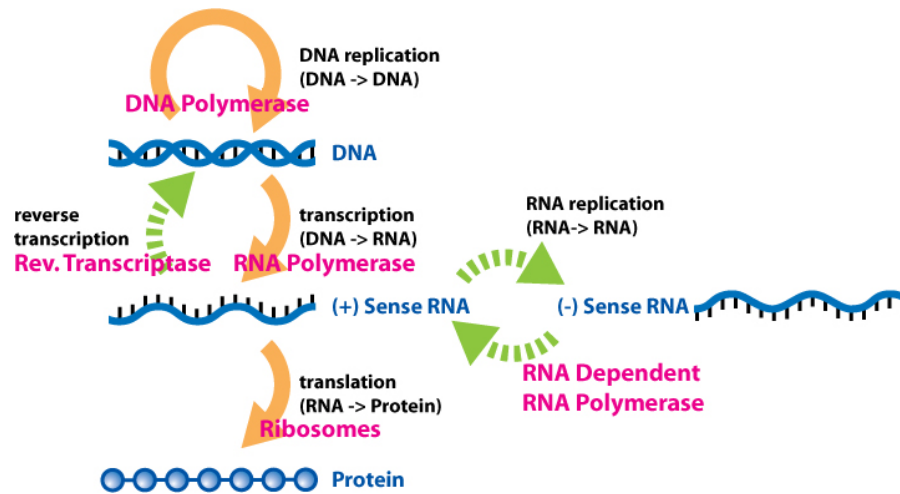
$$(1 \text{ } \mu\text{m})^3 = 10^{-12} \text{ cc} = 10^{-15} \text{ l}$$

$$1/(6 \times 10^{23}) / 10^{-15} \text{ l} = \mathbf{1.6 \text{ nM}}$$

# Virus Reproduction



# Central Dogma

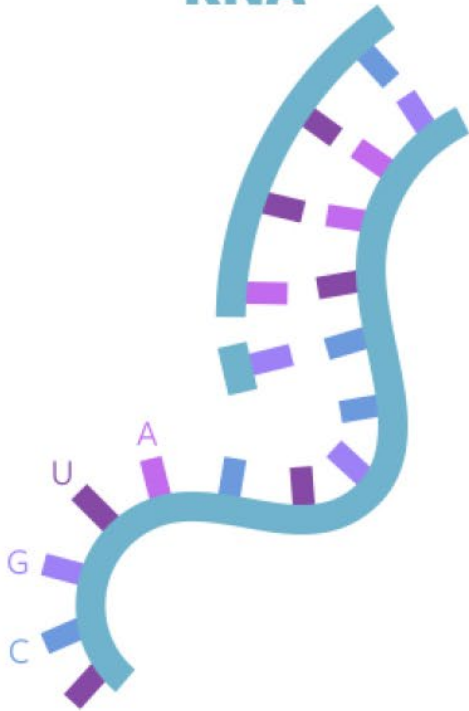




# Definition of Life

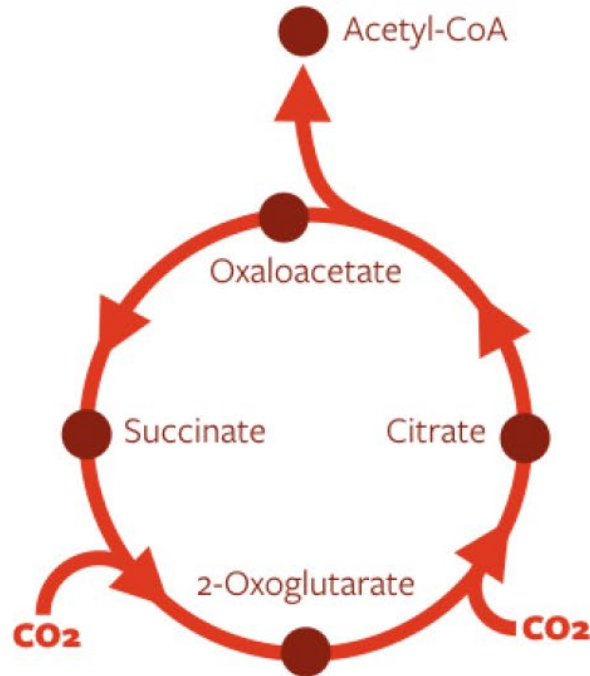
REPLICATION

**RNA**



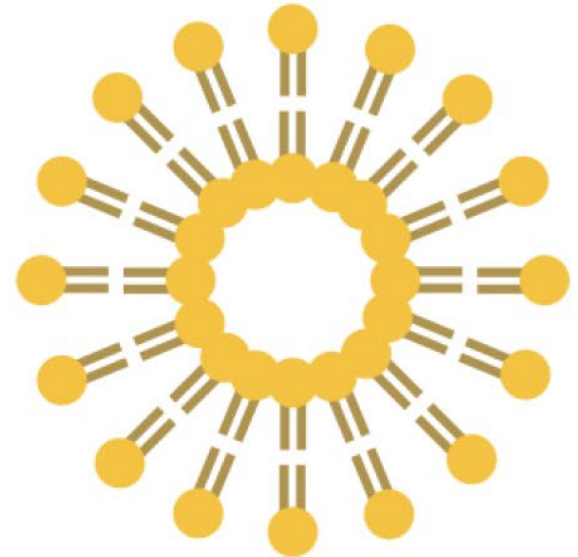
METABOLISM

**rTCA CYCLE**



COMPARTMENTS

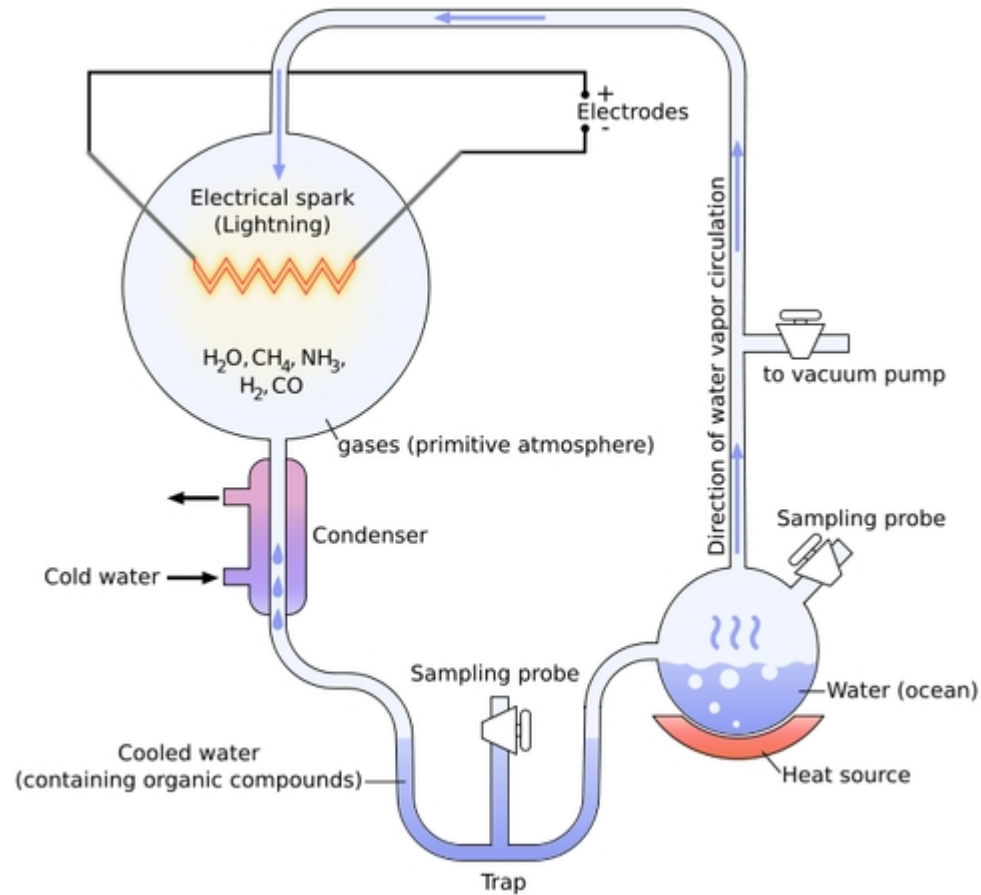
**LIPOSOME**



# Early Life on Earth



# Miller-Urey experiment (1953)



Amino acids

## 1. Primordial Soup Theory

This theory suggests that life began in a "primordial soup" of organic molecules. In the early Earth's oceans, energy from the sun, volcanoes, and lightning helped synthesize simple organic compounds from inorganic substances. The famous Miller-Urey experiment in 1953 supported this idea by producing amino acids from a mixture of water, methane, ammonia, and hydrogen, exposed to electric sparks to simulate lightning.

## 2. Hydrothermal Vent Theory

Another hypothesis posits that life originated at hydrothermal vents on the ocean floor, where mineral-laden water provides a rich source of chemicals. These vents could create the right conditions for organic molecules to form and concentrate, protected from the harsh environment of early Earth's surface. The vents offer a stable, energy-rich environment, with temperature gradients that could drive the formation of complex molecules.

## 3. Panspermia

Panspermia suggests that life, or the building blocks of life, did not originate on Earth but were brought here from space, possibly by meteorites, comets, or cosmic dust. This hypothesis is bolstered by the discovery of amino acids and other organic compounds in meteorites. However, while panspermia could explain how life's building blocks arrived on Earth, it does not explain the origin of life itself.

#### 4. RNA World Hypothesis

The RNA World Hypothesis proposes that before DNA and proteins, life was based on RNA molecules. RNA can store genetic information like DNA and catalyze chemical reactions like enzymes, which makes it a good candidate for the earliest form of life. This theory suggests that self-replicating RNA molecules were the first forms of life, eventually leading to the DNA and protein-based life we see today.

#### 5. Lipid World Hypothesis

This theory focuses on the role of lipids in forming the first cell membranes. It suggests that lipid molecules spontaneously formed bilayers (similar to modern cell membranes) that could encapsulate and protect organic molecules, facilitating the chemical reactions needed for life.

#### 6. Deep-Sea Alkaline Hydrothermal Vent Theory

A variation on the hydrothermal vent theory, this hypothesis suggests that life began at alkaline hydrothermal vents, where warm, pH-neutral water could have mixed with the ocean's more acidic water, creating a natural proton gradient—a driving force for energy production in all living cells today.

# Topics

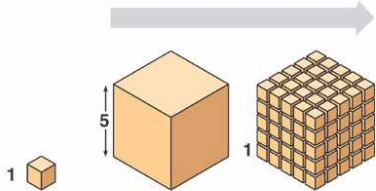
## Fundamental Knowledge and Current Literatures

- Analytical Chemistry
  - Spectroscopic tools
  - Microarray
  - Cell-surface interaction
  - Ultrasensitive detection
- Physical Chemistry
  - Single molecular behavior (Optical and AFM)
  - Optical properties of Q-dot
  - SERS
  - Surface plasmon
- Material Chemistry:
  - Nanomaterials: Q-dot, nanoparticle, DNA assembly
  - Surface functionalization
  - Drug delivery
  - DNA, Protein, Cell interactions
  -

New Development in Nanobiotechnology

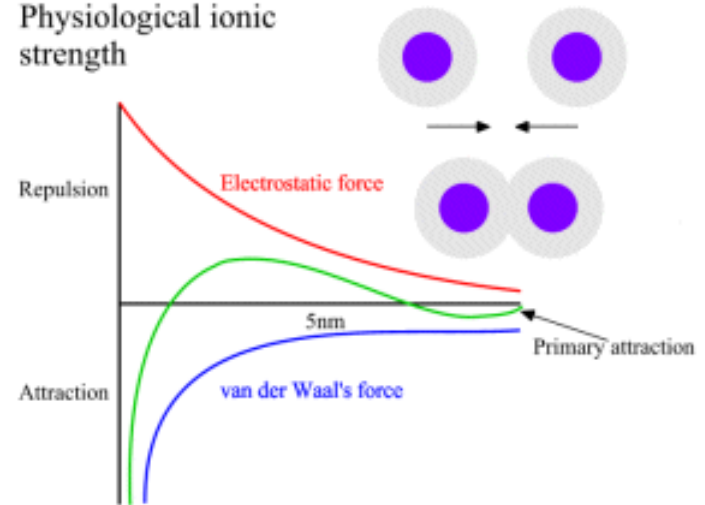
# Properties of Nanomaterials

Surface area increases while total volume remains constant

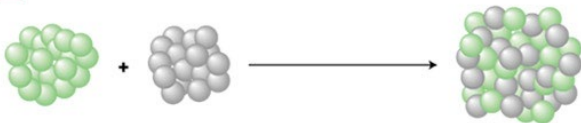


Total surface area (height × width × number of sides × number of boxes)	6	150	750
Total volume (height × width × length × number of boxes)	1	125	125
Surface-to-volume ratio (surface area / volume)	6	1.2	6

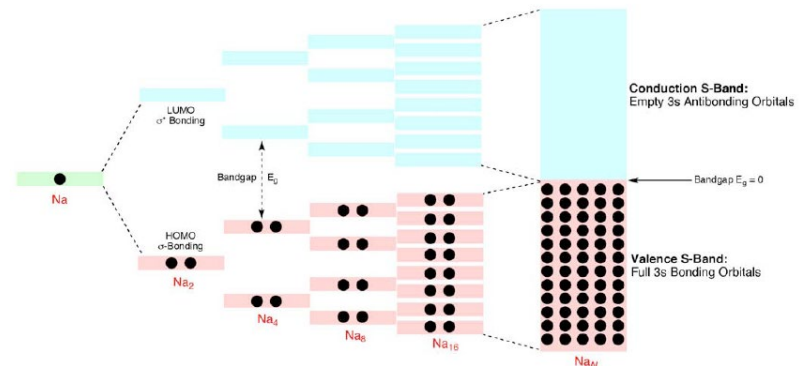
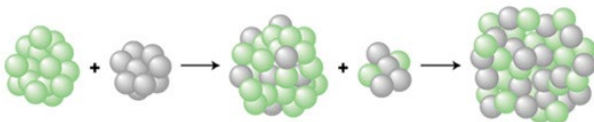
Physiological ionic strength



**a** Coalescence



**b** Ostwald ripening



# Review of General Chemistry, Biochemistry and Cell Biology

TABLE 18.1 Functional Groups of Importance in Biochemical Molecules

Functional Group	Structure	Type of Biomolecule
Amino group	$-\text{NH}_3^+$ , $-\text{NH}_2$	Amino acids and proteins (Sections 18.3, 18.7)
Hydroxyl group	$-\text{OH}$	Monosaccharides (carbohydrates) and glycerol: a component of triacylglycerols (lipids) (Sections 22.4, 24.2)
Carbonyl group	$\begin{array}{c} \text{O} \\ \parallel \\ -\text{C}- \end{array}$	Monosaccharides (carbohydrates); in acetyl group ( $\text{CH}_3\text{CO}$ ) used to transfer carbon atoms during catabolism (Sections 22.4, 21.4, 21.8)
Carboxyl group	$\begin{array}{c} \text{O} \\ \parallel \\ -\text{C}-\text{OH} \end{array}$ , $\begin{array}{c} \text{O} \\ \parallel \\ -\text{C}-\text{O}^- \end{array}$	Amino acids, proteins, and fatty acids (lipids) (Sections 18.3, 18.7, 24.2)
Amide group	$\begin{array}{c} \text{O} \\ \parallel \\ -\text{C}-\text{N}- \\   \end{array}$	Links amino acids in proteins; formed by reaction of amino group and carboxyl group (Section 18.7)
Carboxylic acid ester	$\begin{array}{c} \text{O} \\ \parallel \\ -\text{C}-\text{O}-\text{R} \end{array}$	Triacylglycerols (and other lipids); formed by reaction of carboxyl group and hydroxyl group (Section 24.2)
Phosphates, mono-, di-, tri-	$\begin{array}{c} \text{O} \\ \parallel \\ -\text{C}-\text{O}-\text{P}-\text{O}^- \\   \quad \quad \quad   \\ \quad \quad \quad \quad \quad \text{O}^- \end{array}$ $\begin{array}{c} \text{O} \quad \quad \quad \text{O} \\ \parallel \quad \quad \quad \parallel \\ -\text{C}-\text{O}-\text{P}-\text{O}-\text{P}-\text{O}^- \\   \quad \quad \quad   \quad \quad \quad   \\ \quad \quad \quad \quad \quad \text{O}^- \quad \quad \quad \text{O}^- \end{array}$ $\begin{array}{c} \text{O} \quad \quad \quad \text{O} \quad \quad \quad \text{O} \\ \parallel \quad \quad \quad \parallel \quad \quad \quad \parallel \\ -\text{C}-\text{O}-\text{P}-\text{O}-\text{P}-\text{O}-\text{P}-\text{O}^- \\   \quad \quad \quad   \quad \quad \quad   \quad \quad \quad   \\ \quad \quad \quad \quad \quad \text{O}^- \quad \quad \quad \text{O}^- \quad \quad \quad \text{O}^- \end{array}$	ATP and many metabolism intermediates (Sections 17.8, 21.5, and throughout metabolism sections)
Hemiacetal group	$\begin{array}{c}   \\ -\text{C}-\text{OH} \\   \\ \text{OR} \end{array}$	Cyclic forms of monosaccharides; formed by a reaction of carbonyl group with hydroxyl group (Sections 16.7, 22.4)
Acetal group	$\begin{array}{c}   \\ -\text{C}-\text{OR} \\   \\ \text{OR} \end{array}$	Connects monosaccharides in disaccharides and larger carbohydrates; formed by reaction of carbonyl group with hydroxyl group (Sections 16.7, 22.7, 22.9)

Amino Acid  
Nuclear Acid  
Carbohydrate  
Lipid



# Method of the Year 2020: spatially resolved transcriptomics

Spatially resolved transcriptomics methods are changing the way we understand complex tissues.

# Method of the Year 2019: Single-cell multimodal omics

Multimodal omics measurement offers opportunities for gaining holistic views of cells one by one.

# Method of the Year 2018: Imaging in freely behaving animals

Neuronal imaging in unrestrained animals has expanded the range of behaviors amenable to circuit-level studies in several model organisms.

# Method of the Year 2017: Organoids

The ability to prod stem cells into three-dimensional tissue models makes for a powerful way to study human biology. But these exciting tools are still works in progress.

# Method of the Year 2016: Epitranscriptome analysis

Chemical modifications on ribonucleotides are being profiled with increased efficiency and appreciated as important regulatory features.

# Method of the Year 2015

The end of 'blob-ology': single-particle cryo-electron microscopy (cryo-EM) is now being used to solve macromolecular structures at high resolution.

Imaging: 2018, 2015, 2014, 2010, 2008

DNA Sequencing: 2022, 2020, 2019, 2016, 2013

Organoid: 2017

# Method of the Year 2014

Light-sheet fluorescence microscopy can image living samples in three dimensions with relatively low phototoxicity and at high speed.

# Method of the Year 2013

Methods to sequence the DNA and RNA of single cells are poised to transform many areas of biology and medicine.

# Method of the Year 2010

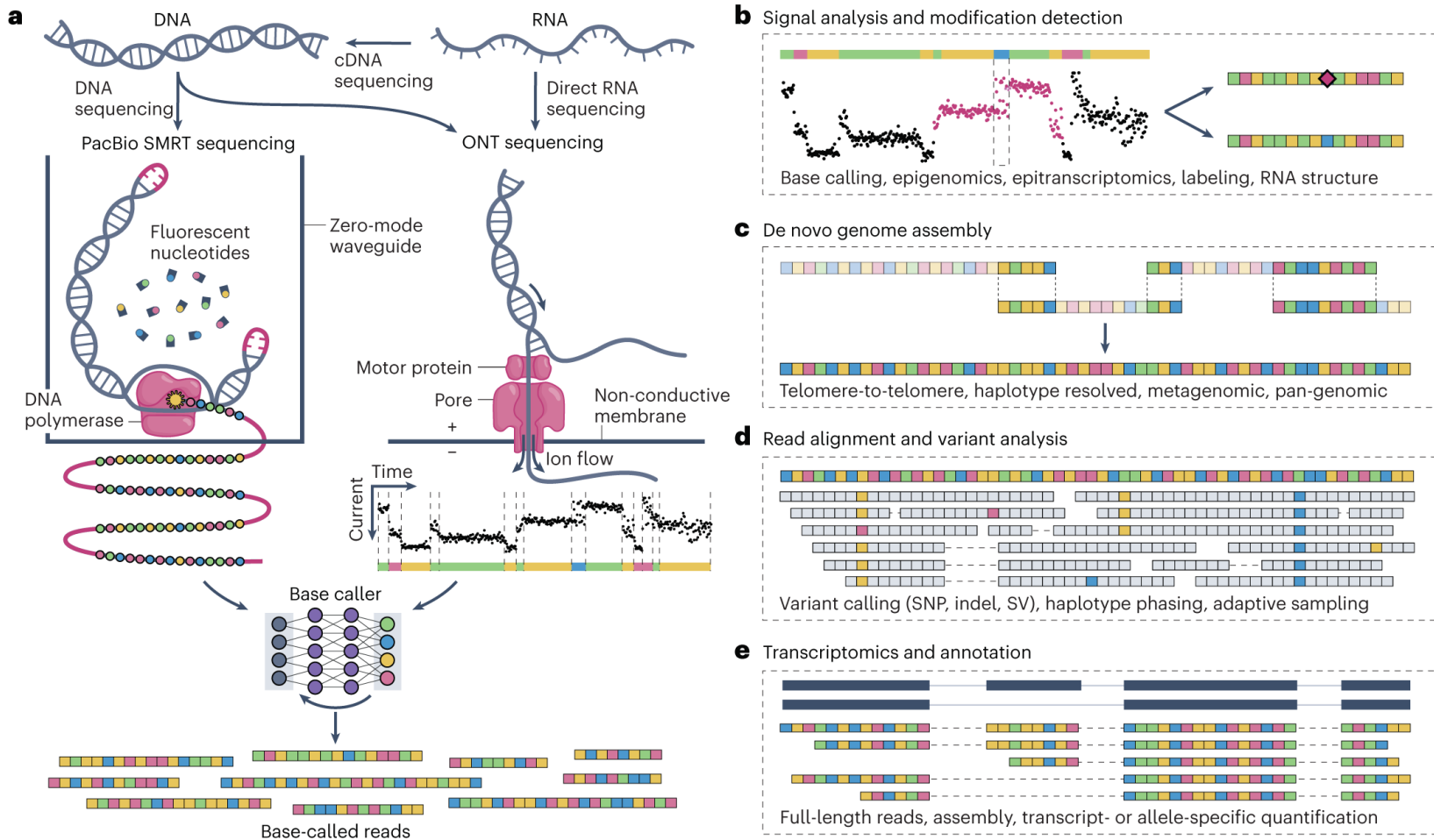
With the capacity to control cellular behaviors using light and genetically encoded light-sensitive proteins, optogenetics has opened new doors for experimentation across biological fields.

# Method of the Year 2008

With its tremendous potential for understanding cellular biology now poised to become a reality, super-resolution fluorescence microscopy is our choice for Method of the Year.

# METHOD OF THE YEAR: LONG-READ SEQUENCING

Year 2022



# Method of the Year 2021: Protein structure prediction

Protein structure predictions to atomic accuracy with AlphaFold

