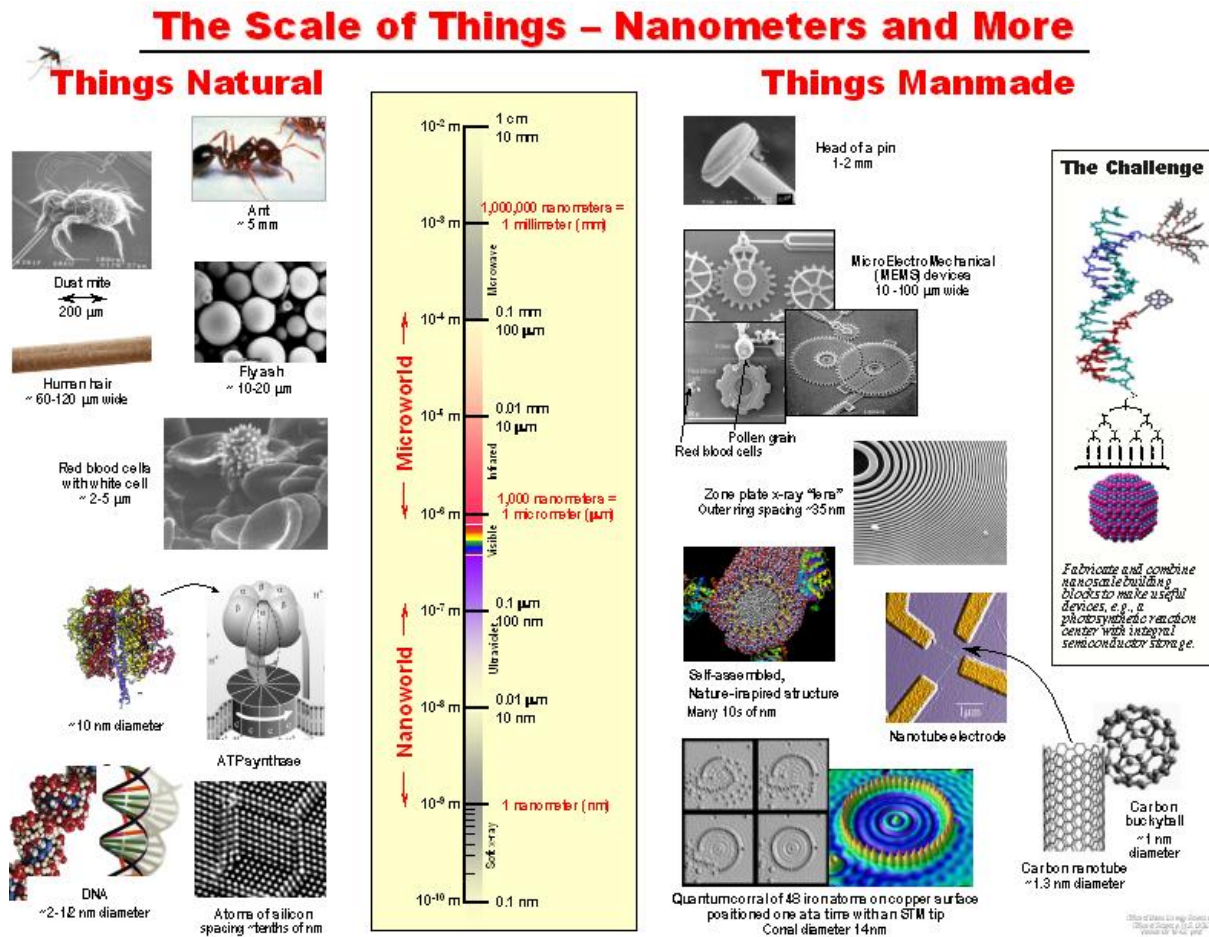
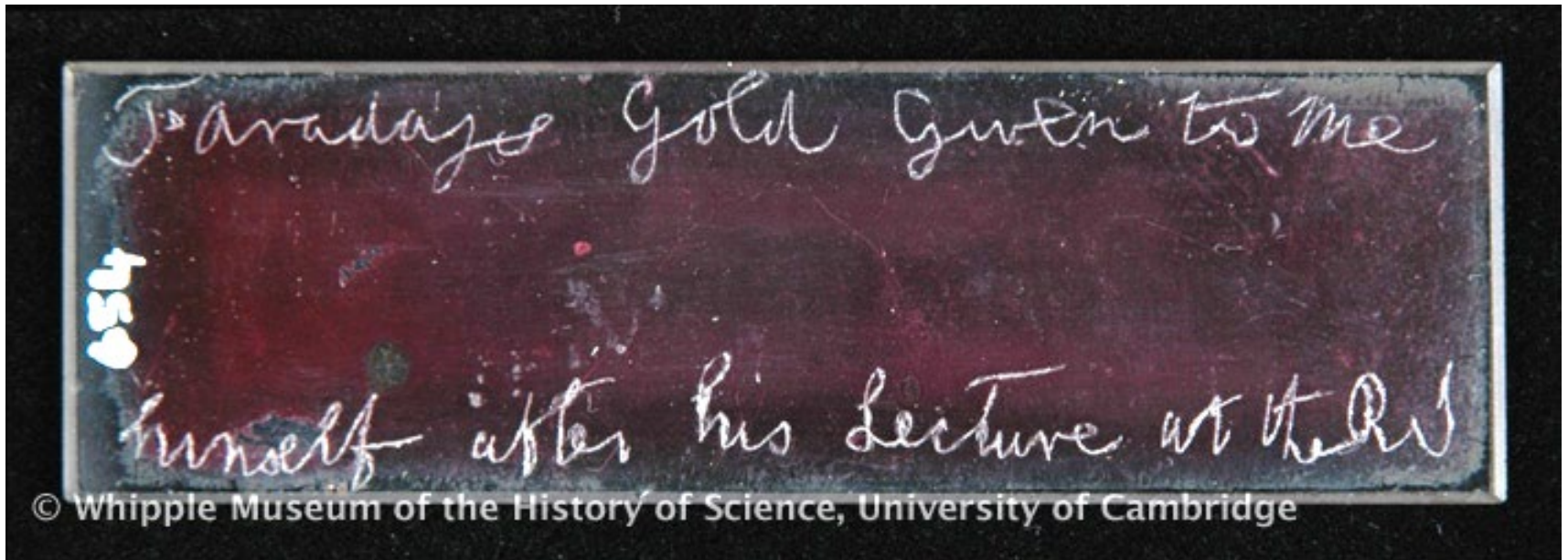


# What is nano?



# Faraday's Gold Sol



1856  
20-40 nm gold

# 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

## Method of the Year 2020: spatially resolved transcriptomics

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

Imaging: 2018, 2015, 2014, 2010, 2008

DNA Sequencing: 2020, 2019, 2016, 2013

Organoid: 2017

## 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 2014

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

## 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 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 2015

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

## Method of the Year 2010

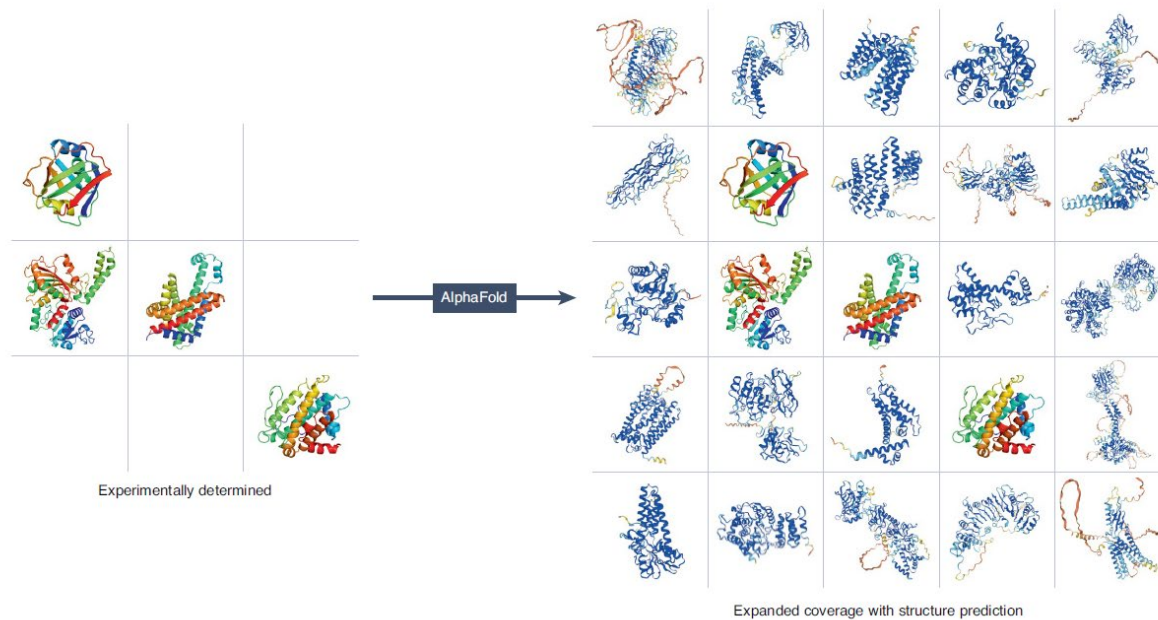
With the capacity to control cellular behaviors using light and genetically encoded light-sensitive proteins, optogenetics has opened new doors for experimentation across biological fields.

## 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 2021: Protein structure prediction

Protein structure predictions to atomic accuracy with AlphaFold





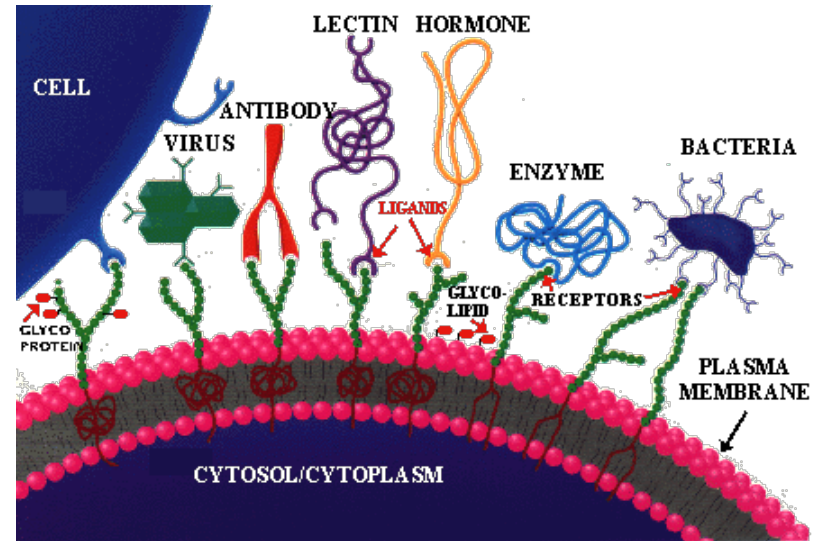
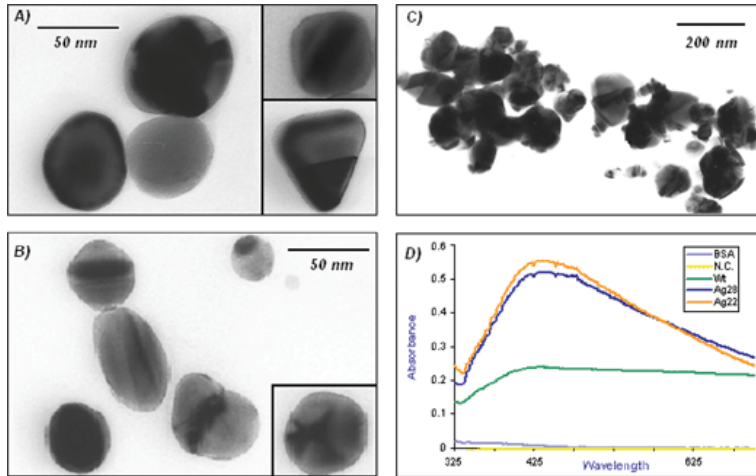
# Review of General Chemistry, Biochemistry and Cell Biology

TABLE 18.1 Functional Groups of Importance in Biochemical Molecules

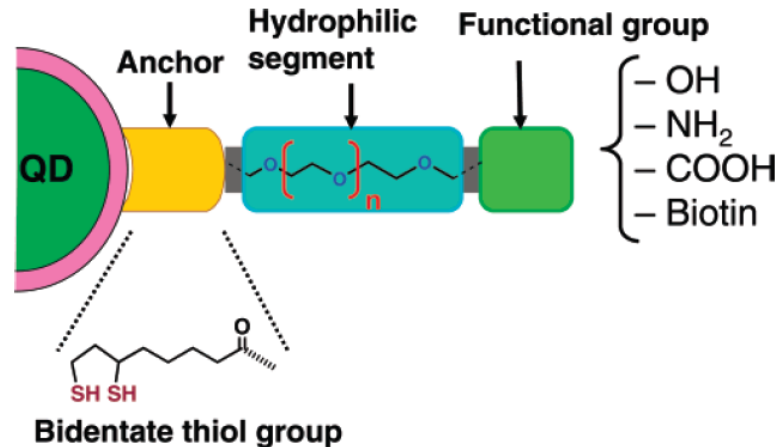
| Functional Group             | Structure   | Type of Biomolecule  |
|------------------------------|---|--|
| Amino group                  | $-\text{NH}_3^+$ , $-\text{NH}_2$   | Amino acids and proteins (Sections 18.3, 18.7)   |
| Hydroxyl group               | $-\text{OH}$  | Monosaccharides (carbohydrates) 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- | $\begin{array}{c} \text{O} \\ \parallel \\ -\text{C}-\text{O}-\text{P}-\text{O}^- \\ \parallel \\ \text{O}^- \end{array}$<br>$\begin{array}{c} \text{O} \quad \text{O} \\ \parallel \quad \parallel \\ -\text{C}-\text{O}-\text{P}-\text{O}-\text{P}-\text{O}^- \\ \parallel \quad \parallel \\ \text{O}^- \quad \text{O}^- \end{array}$<br>$\begin{array}{c} \text{O} \quad \text{O} \quad \text{O} \\ \parallel \quad \parallel \quad \parallel \\ -\text{C}-\text{O}-\text{P}-\text{O}-\text{P}-\text{O}-\text{P}-\text{O}^- \\ \parallel \quad \parallel \quad \parallel \\ \text{O}^- \quad \text{O}^- \quad \text{O}^- \end{array}$ | 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

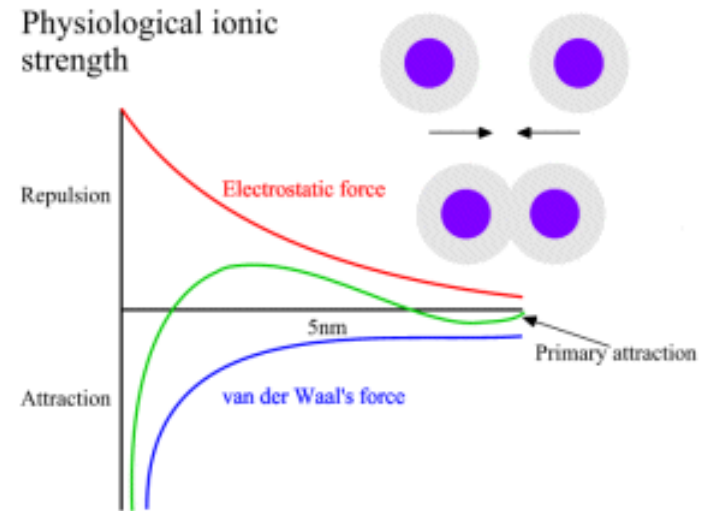
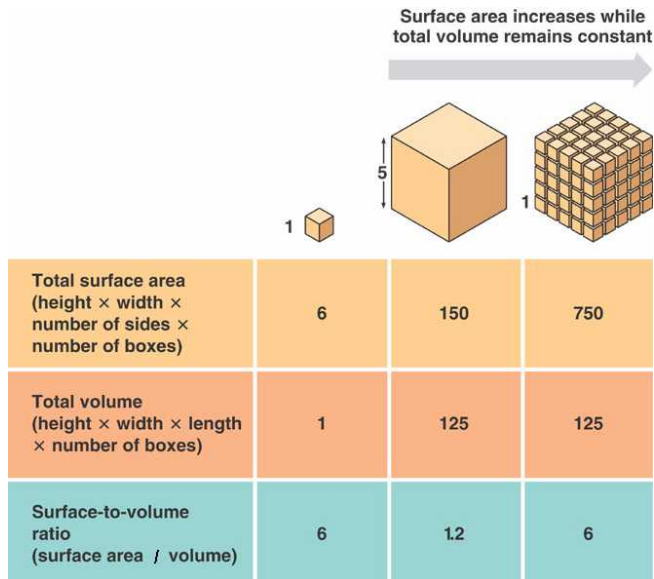
# Synthesis of Nanoparticles and Surface Modifications



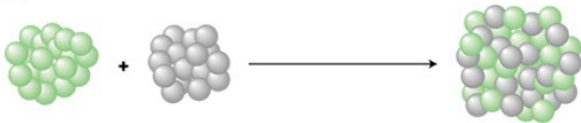
**Scheme 1.** Modular Design of Hydrophilic Ligands with Terminal Functional Groups Used in This Study



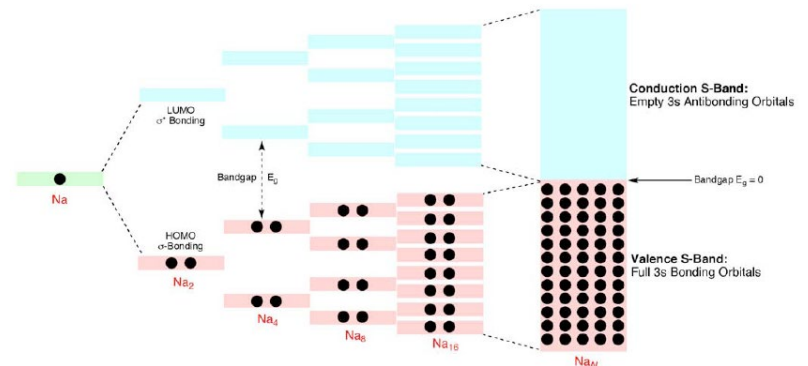
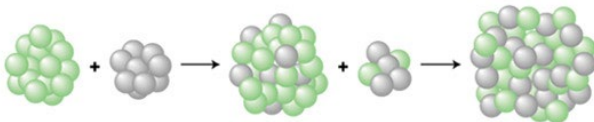
# Properties of Nanomaterials



**a** Coalescence



**b** Ostwald ripening



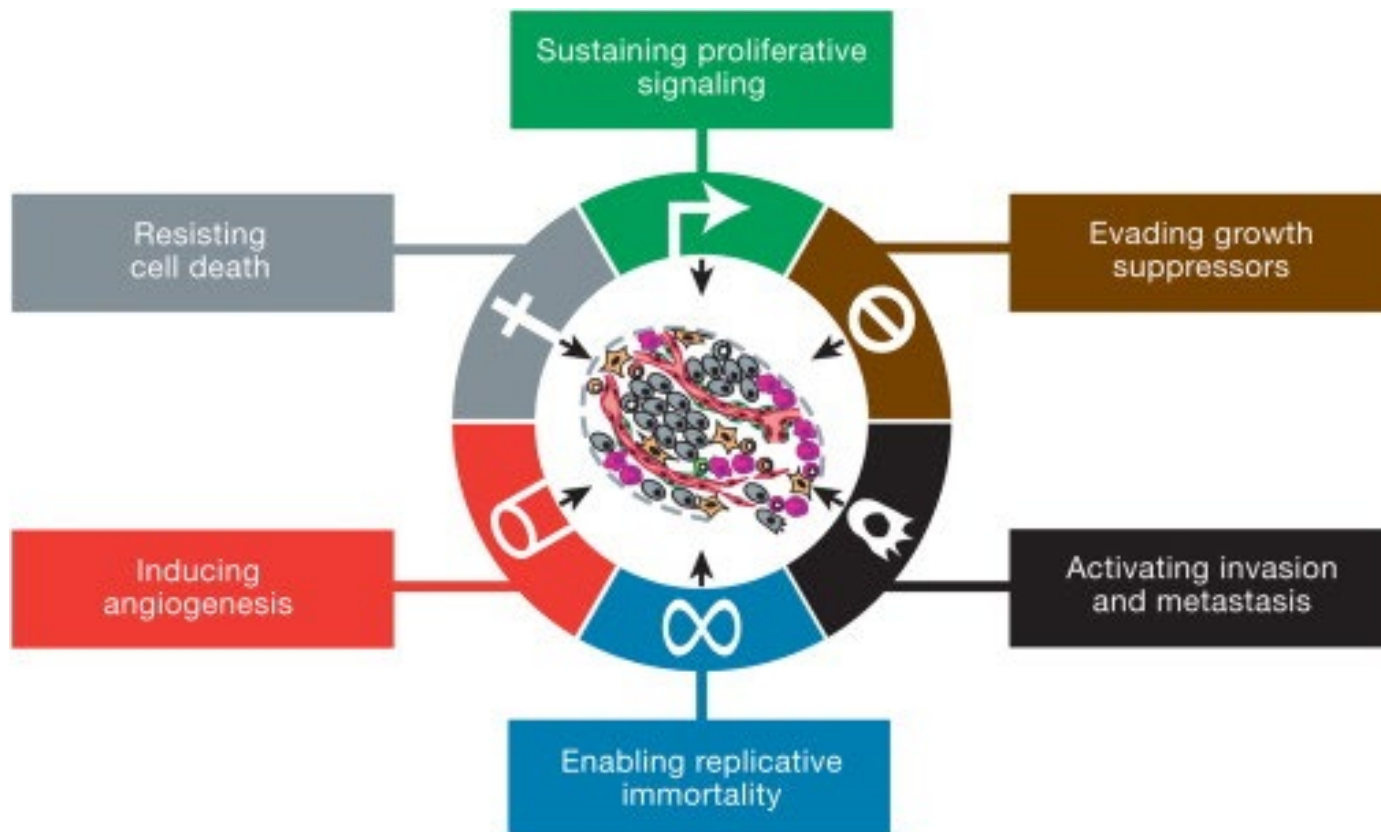


# Nanomaterials for Biodiagnostic

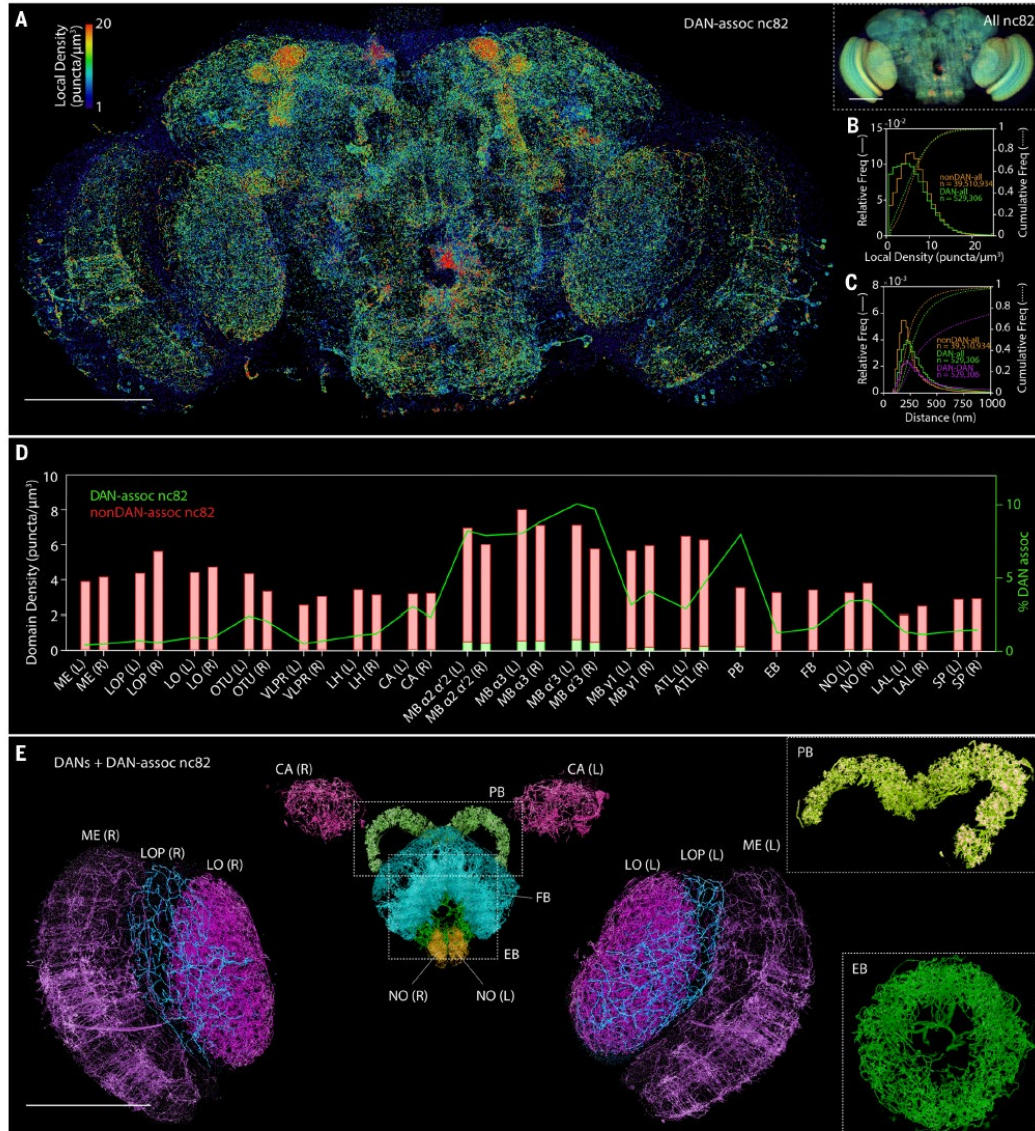
- Nucleic Acid
  - Genetic information for identification
  - Diseases, bacterium, virus, pathogen
  - PCR with molecular fluorophore, State of the Art
  - Expansive, Non-portable, Non-multiplexing
- Proteins
  - Cancers and diseases, unusual high concentration of marker
  - ELISA ( $\sim$ pM) with molecular fluorophore
  - No PCR version

# Nanomedicine

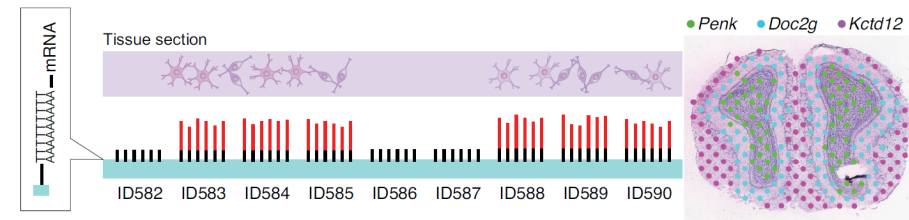
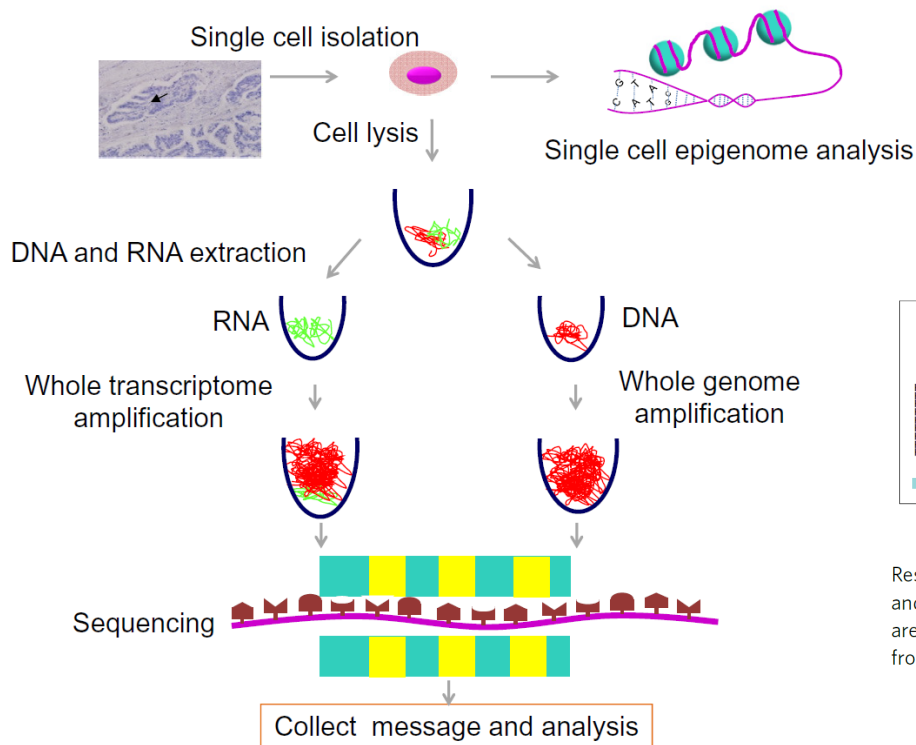
## Cancer Hallmark



# Imaging and Sequencing



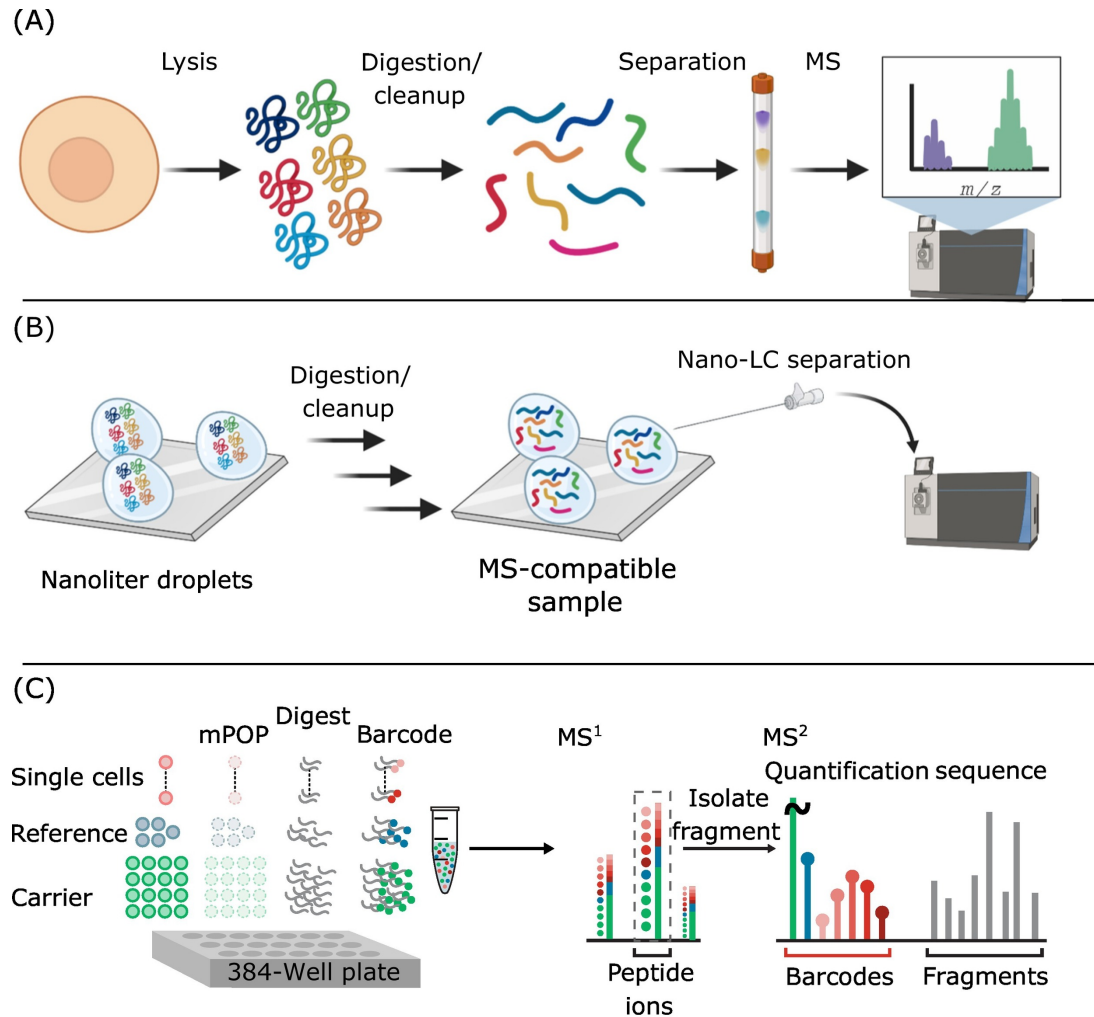
# Single Cell Sequencing



Researchers in Sweden developed an approach in which fixed, stained tissue is imaged, permeabilized and the mRNAs attach to an array of barcoded oligos. The RNAs are reverse-transcribed; the cDNAs are sequenced and yield spatially resolved transcriptomic information. Credit: Adapted with permission from ref. <sup>4</sup>, AAAS

**Fig. 1.** Single-cell sequencing of a tumor cell. A tumor specimen is obtained by surgical excision and single cells are isolated by one of the several methods shown in Fig. 2. The individual cancer cell can be used for epigenome sequencing directly or lysed to extract the genetic material (DNA and RNA), which is in turn amplified by the methods shown in Fig. 3. Then, the amplified DNA and RNA are sequenced by single-cell sequencing technology and the result data are analyzed to provide insights into the molecular mechanisms underlying intratumor heterogeneity.

# Single Cell Proteomic





# Multiple rereads of single proteins at single-amino acid resolution using nanopores

**Henry Brinkerhoff<sup>1</sup>, Albert S. W. Kang<sup>1</sup>, Jingqian Liu<sup>2</sup>, Aleksei Aksimentiev<sup>2</sup>, Cees Dekker<sup>1\*</sup>**

