EPFL
École polytechnique fédérale de Lausanne

CHEMINA
Laboratory of Chemical Nanotechnology

Probing Functional Interfaces
Lesson 10

MSE 304

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Plan of the Course: Fundamentals, Characterization, and Applications

1: Intro to Surfaces & Interfaces

2: Surfaces in the Real World - Adsorption

3: Surface Energetics & Interfacial Phenomena

4: Atomic Structure of Real Surfaces

5: Solid-Solid Interfaces

6: From Ideal Planes to Real Materials (Recap)

7: Characterization of Surfaces & Interfaces

8: Surface Chemistry

9: Surface Patterning and Polymer Chemistry

10: Probing Functional Interfaces

11: Applications of Surfaces & Interfaces

12: Biosensor Fundamentals

13: Biosensing applications

14: Chemistry of Semiconductor Surfaces and Beyond

Recap from Lesson 9: Patterning for Spatial Control

Inkjet printing

~ 50 – 100 µm

Microfluidic patterning

~10 – 100 µm

Microcontact printing

~1 – 10 µm

Chemical lift-off lithography

~10 – 50 nm

Spatial limit

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Recap from Lesson 9

- Functional groups on assembled monolayers (SAMs) can be coupled to other biomolecules

- Nonspecific protein binding on surfaces governed by thermodynamic mechanisms that is surface dependent (neutral, charged, zwitterionic)

- We can control protein adsorption through polymer brushes with specific properties

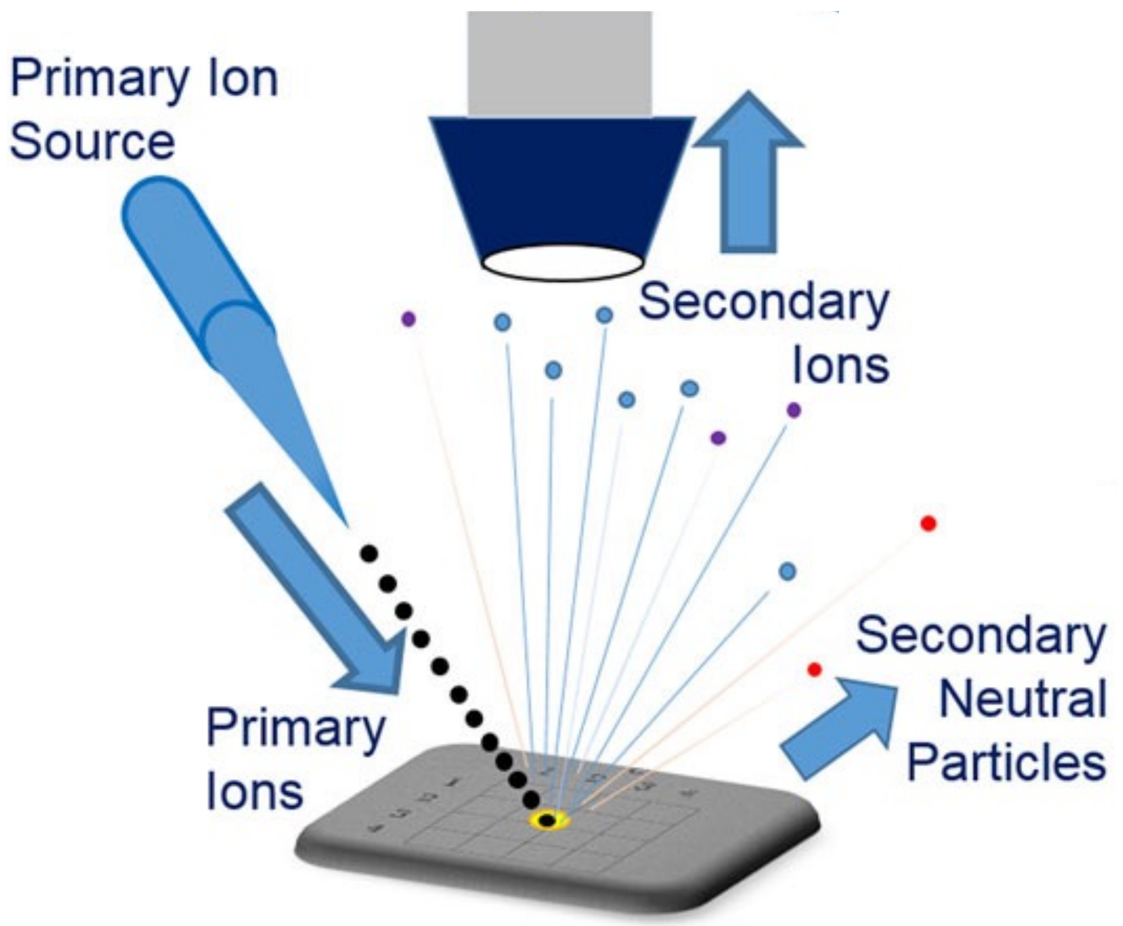
- We discussed the challenges (biosensing) and opportunities (lubricant) of protein adsorption

Outline of Lesson 10

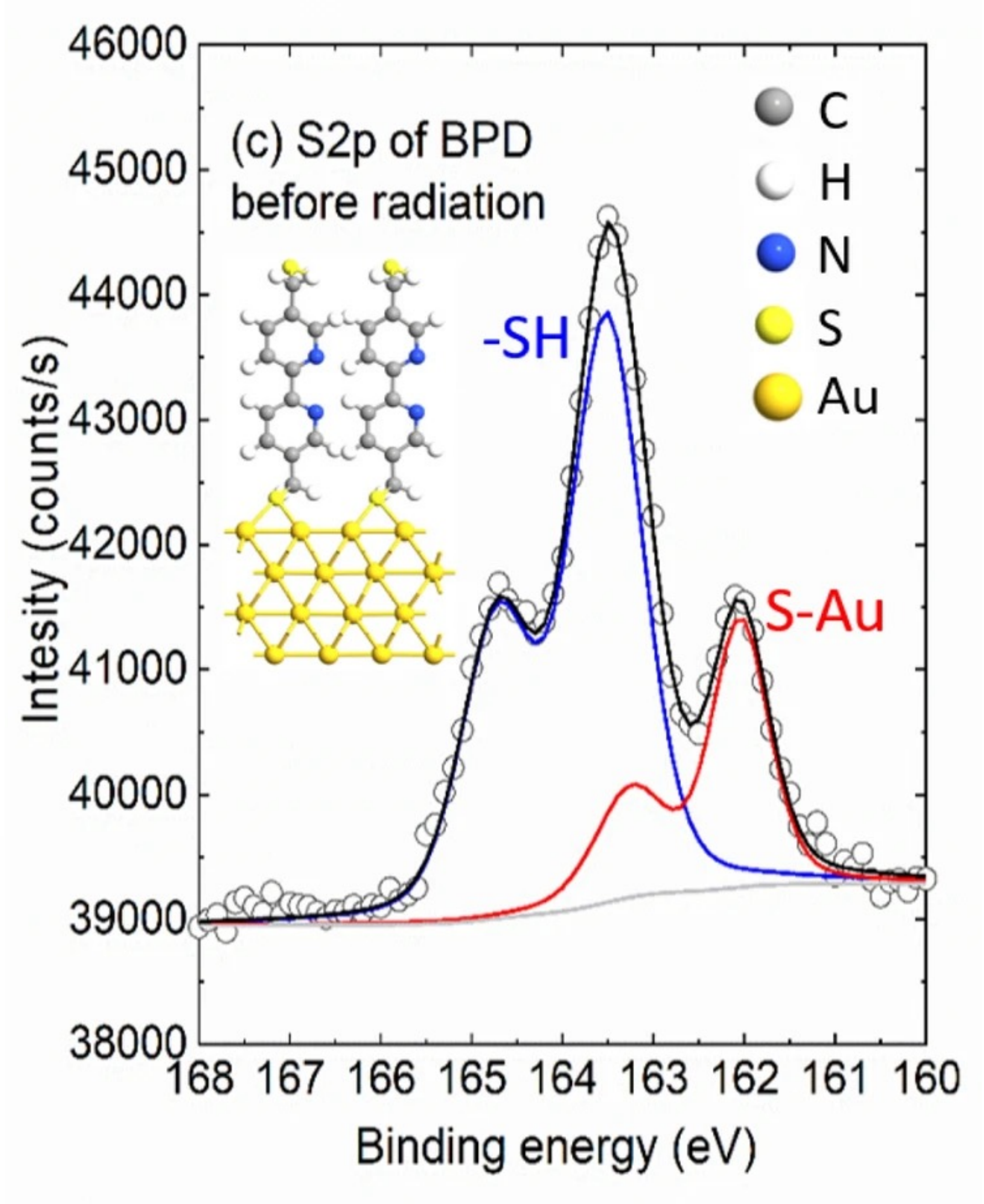
- Characterization techniques that enable extraction of surface properties
- **Atomic force microscopy** – from images to mechanical interactions
- **Fluid force microscopy** – interacting with cells
- **Quartz crystal microbalance** – monitoring surface dynamics
- **Ellipsometry** – measuring thickness of surface layers
- **Surface plasmon resonance + optical waveguide lightmode spectroscopy**

We Have Seen Many Surface Characterization Tools So Far…

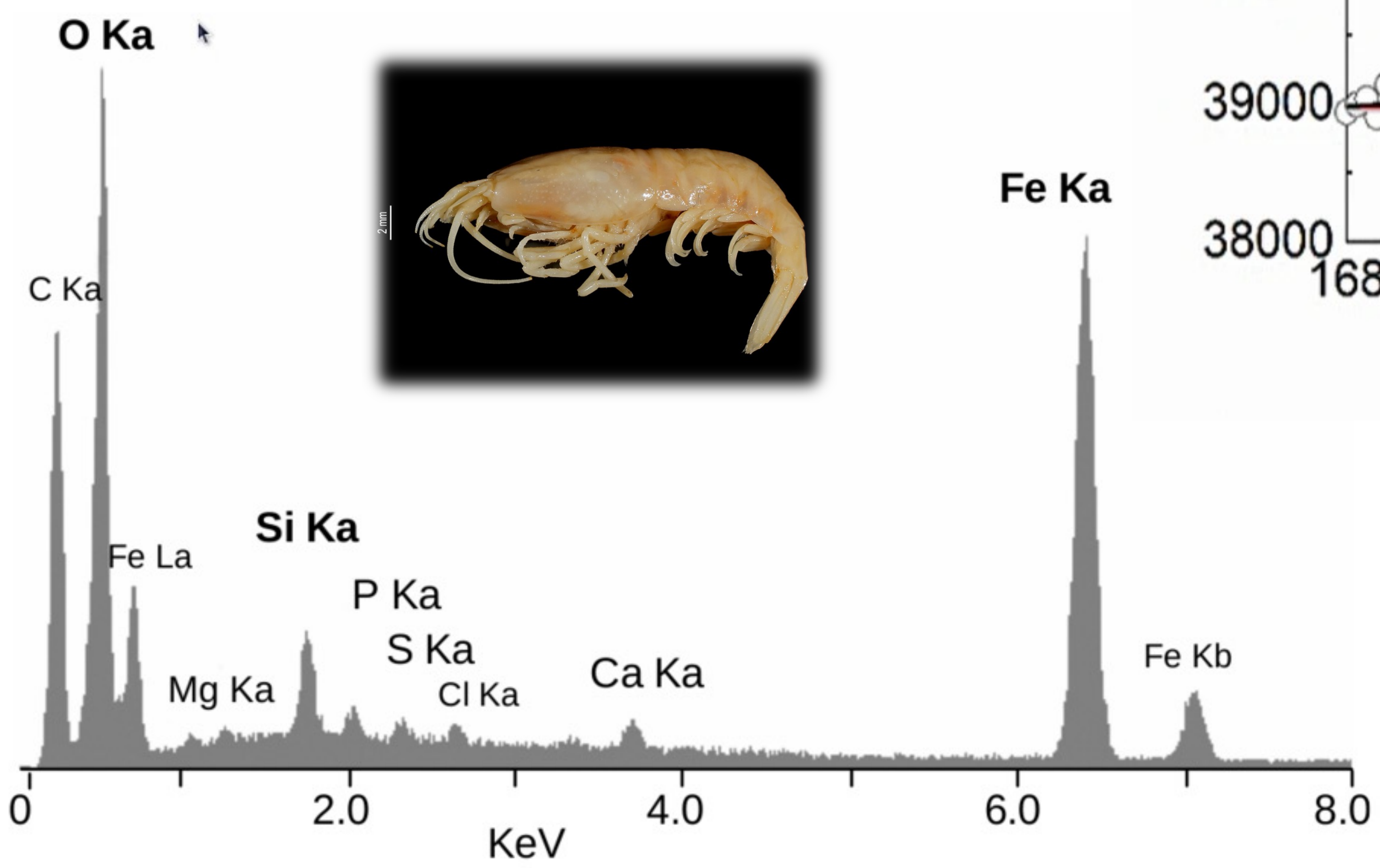
SIMS



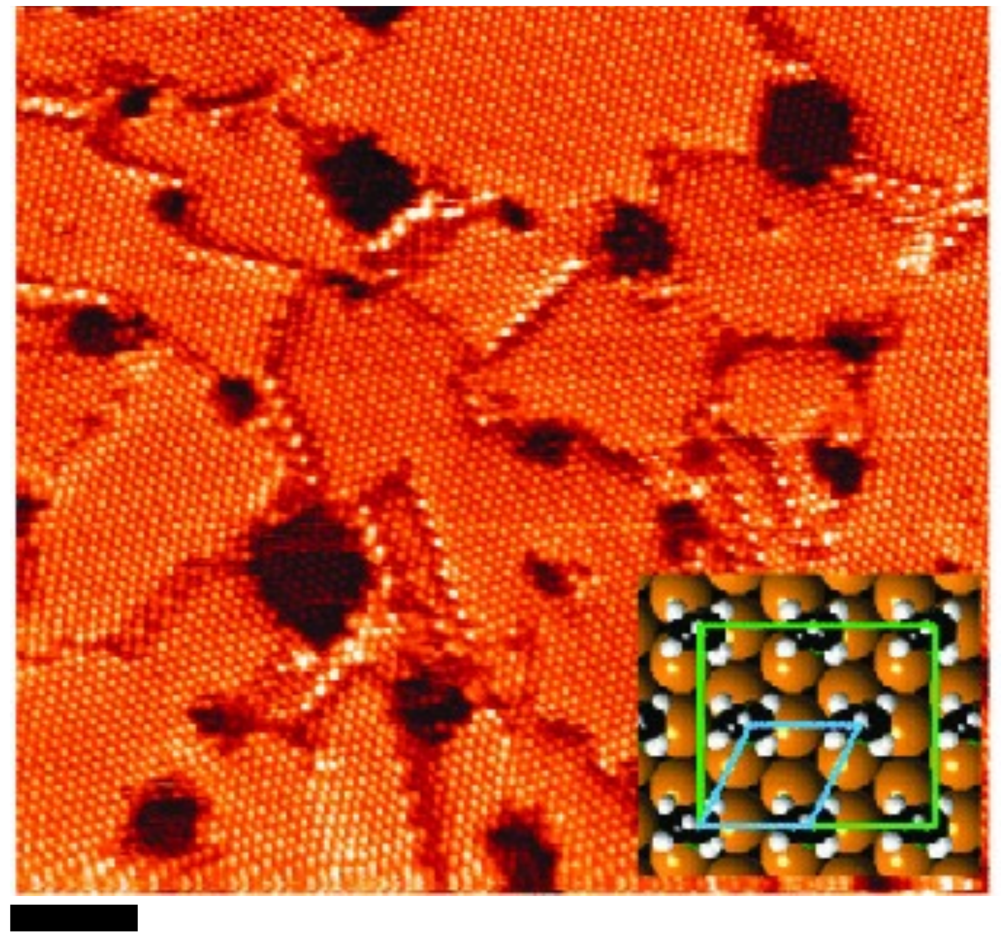
XPS



EDX

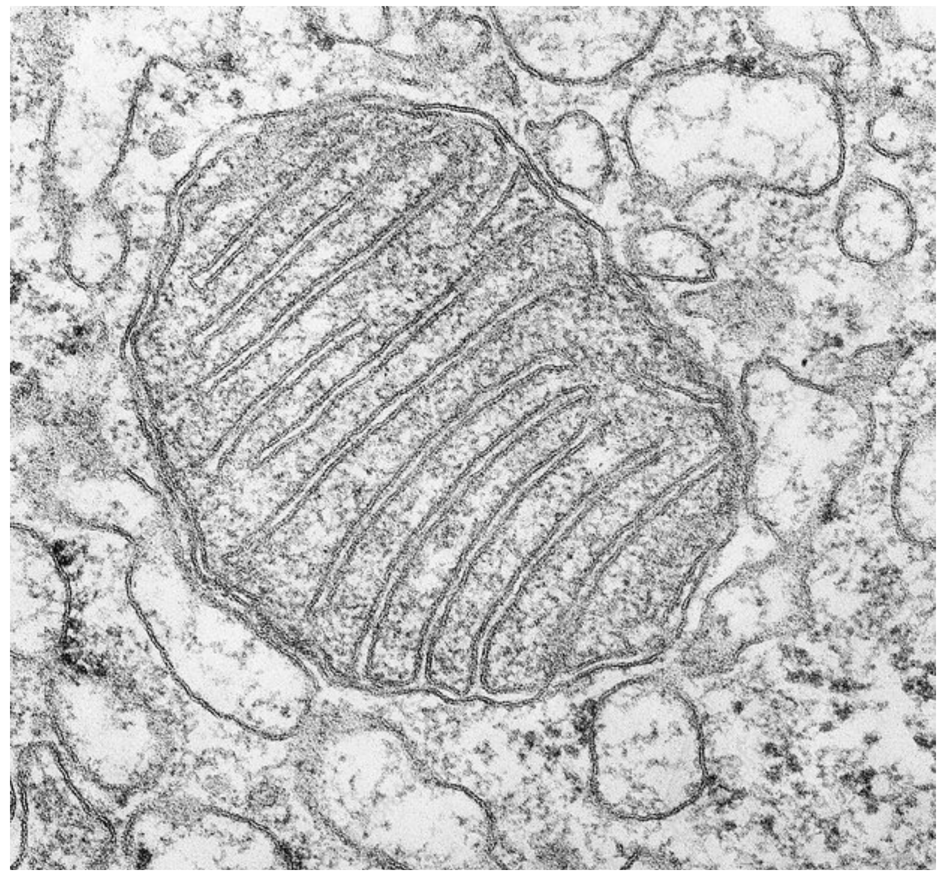


STM

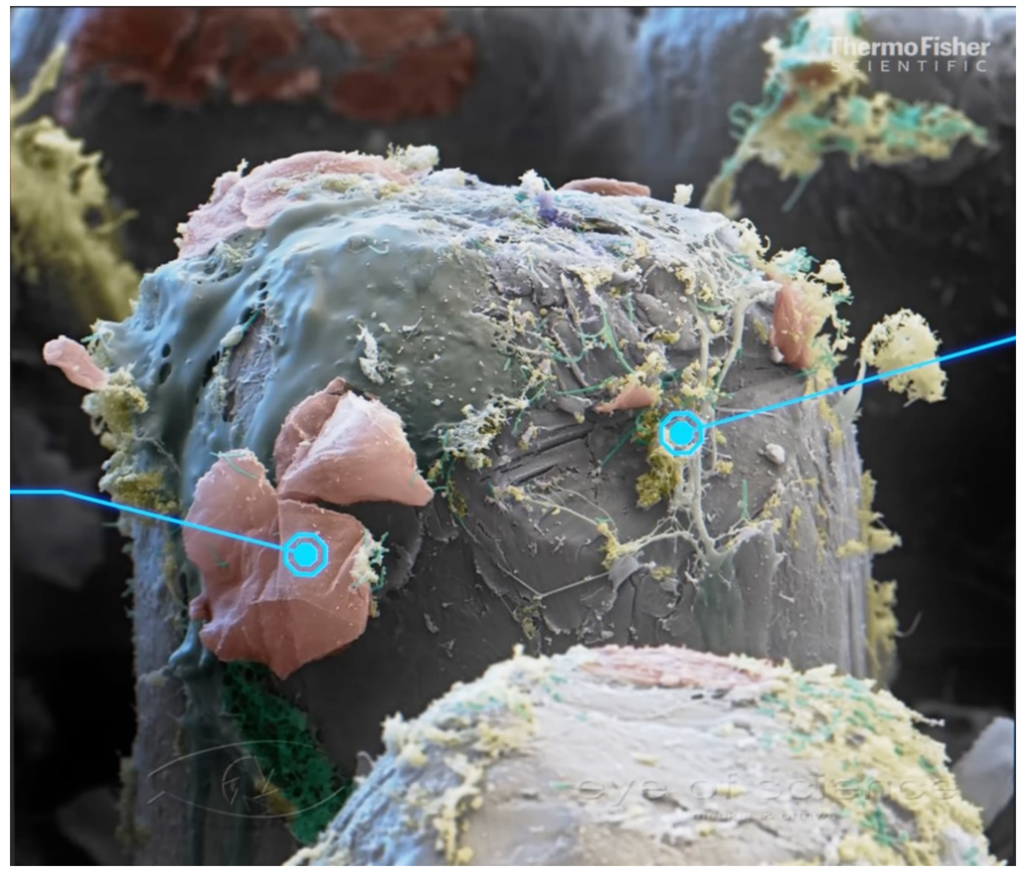


5 nm

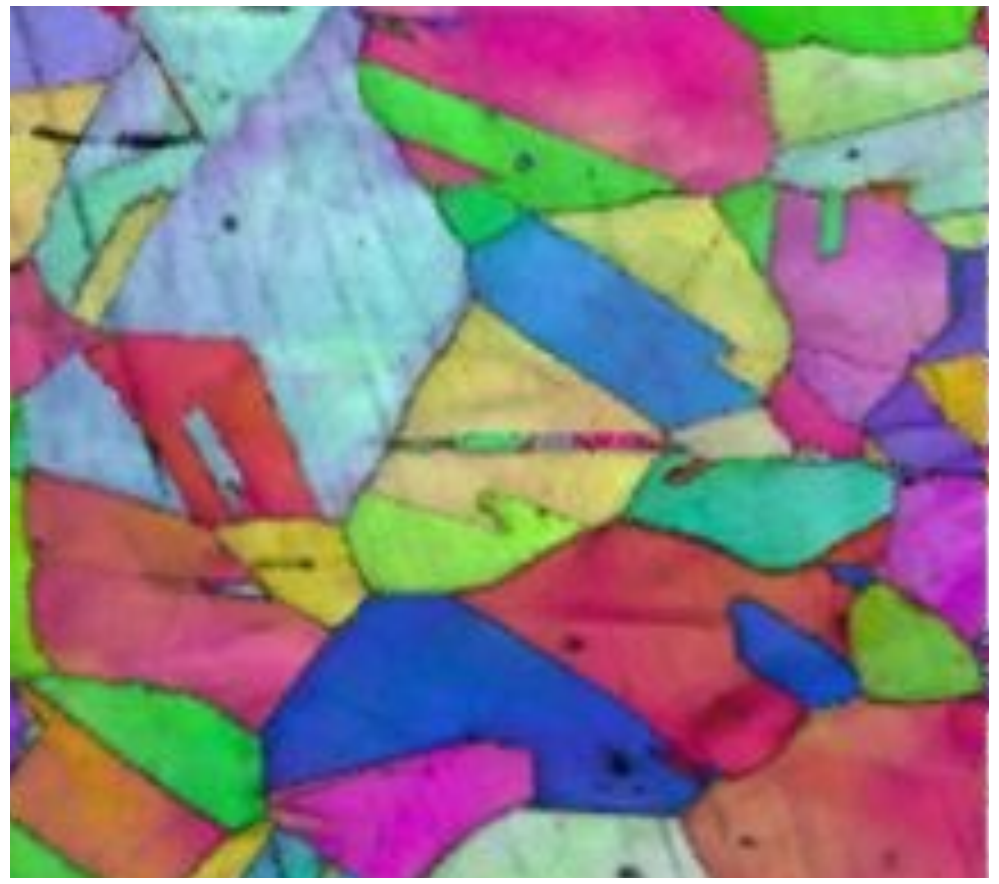
TEM



SEM



EBSD



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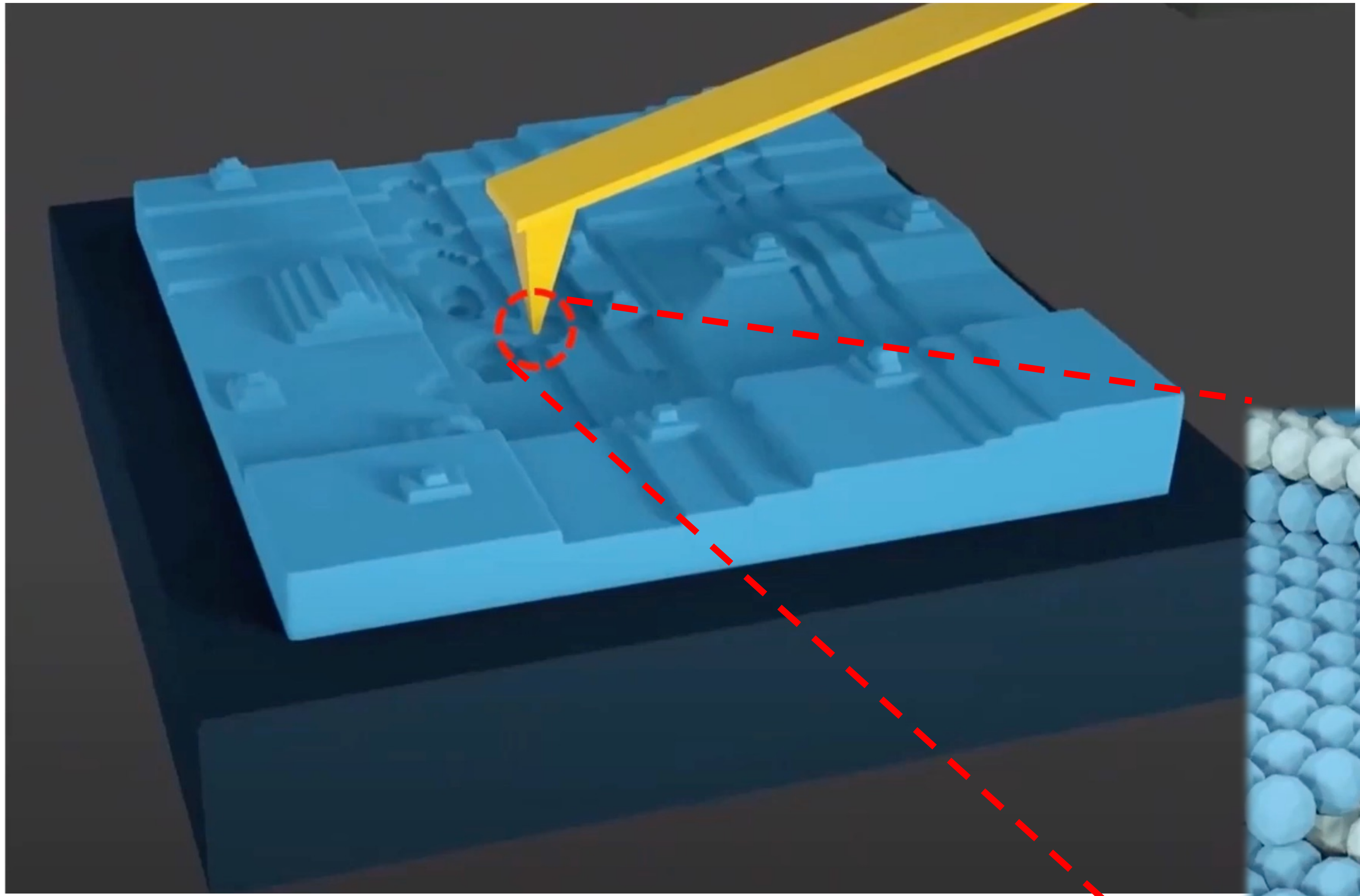
Atomic Force Microscopy (AFM): From Images to Interactions

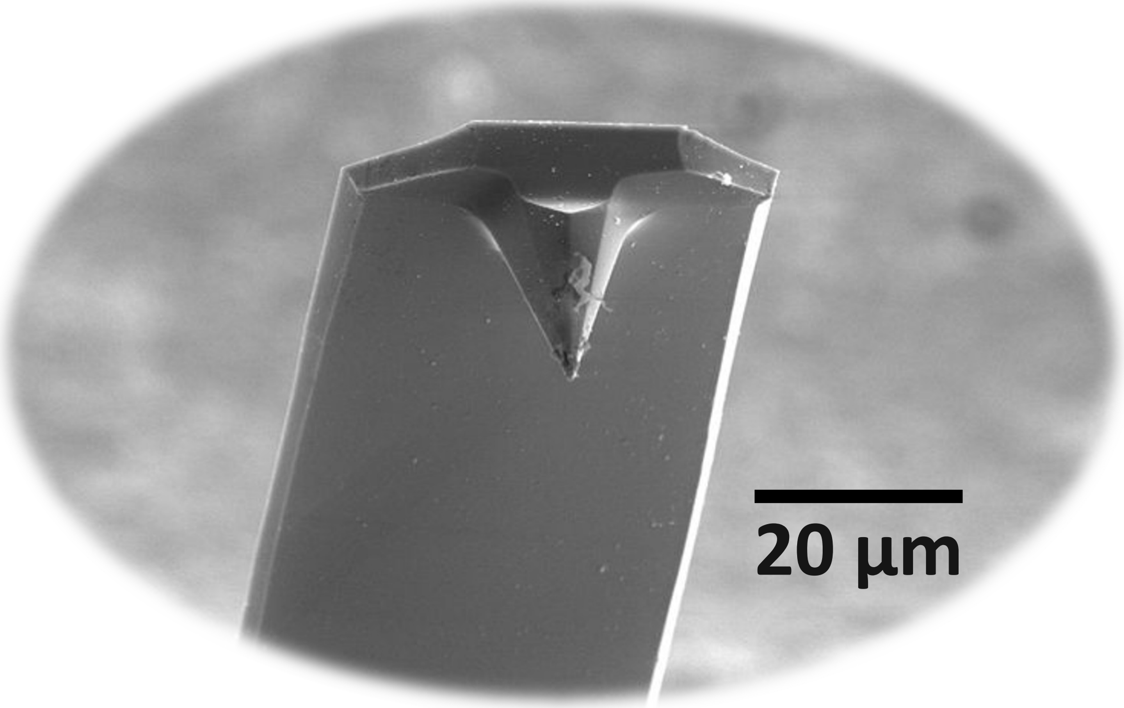
AFM measurements are extremely sensitive to vibrations:

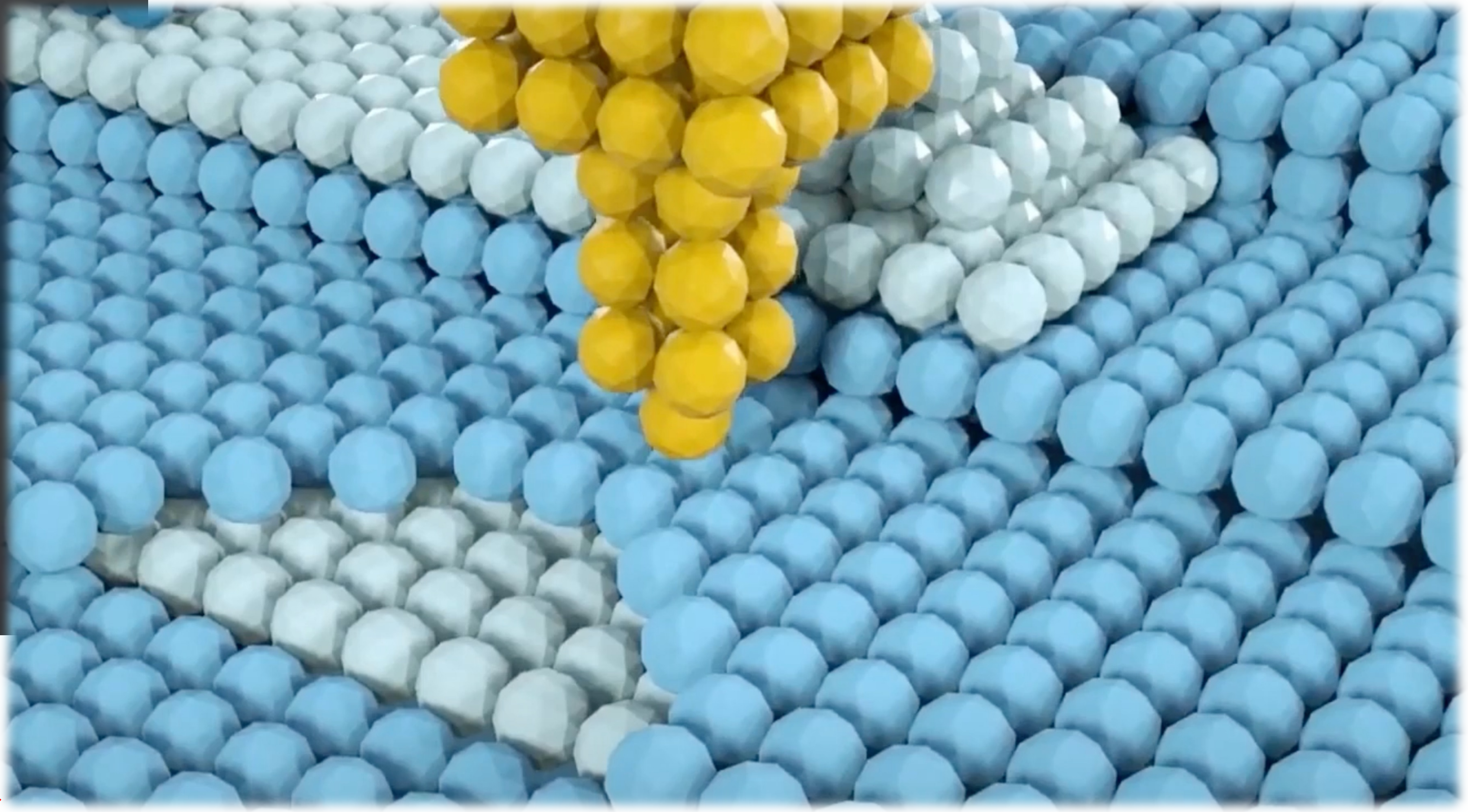
- Vibration isolation in heavy enclosed box
  - Acoustic isolation from sound waves
- Thermal stability (constant temperature)
  - Airflow control with closable box

Atomic Force Microscopy (AFM): From Images to Interactions



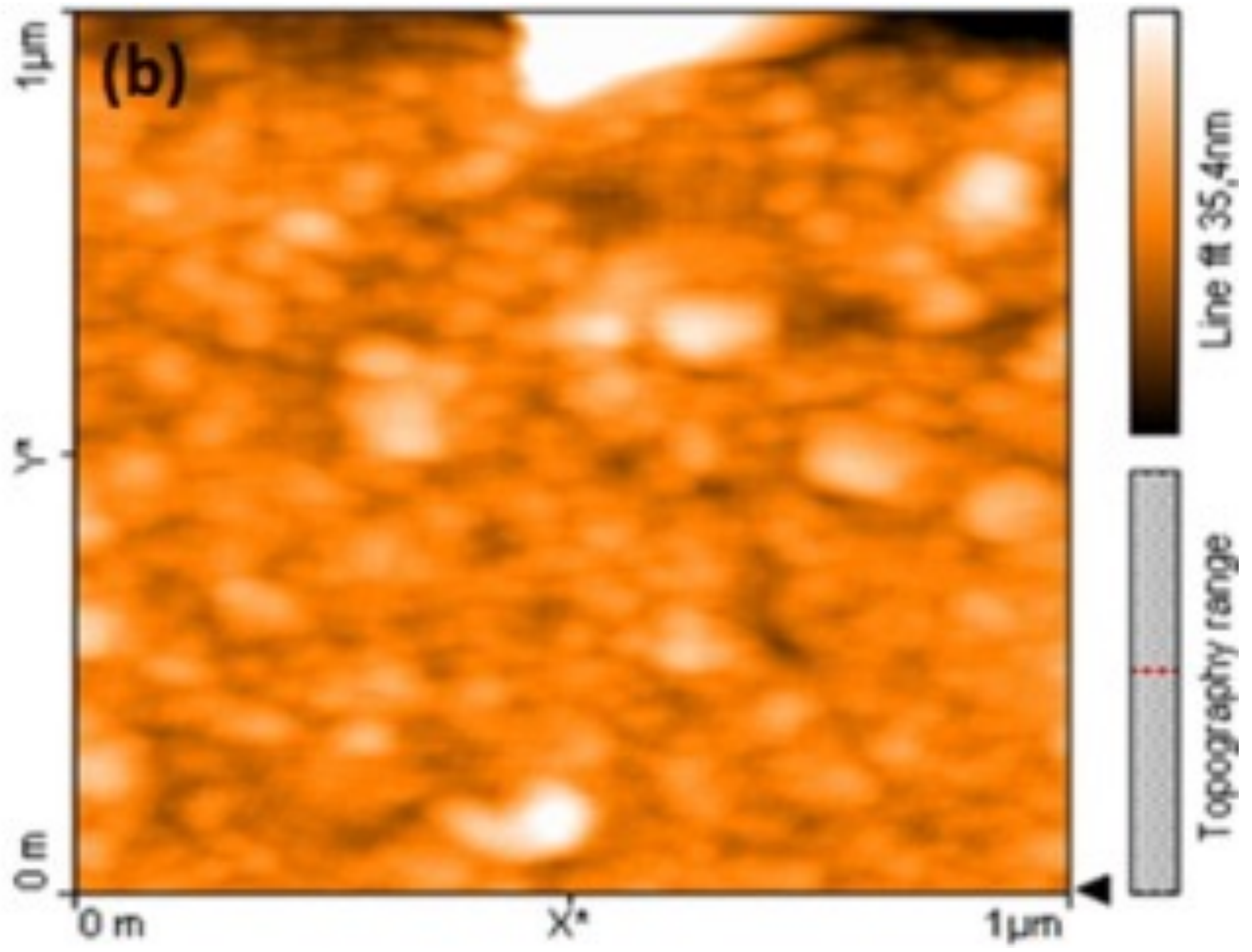
AFM cantilever

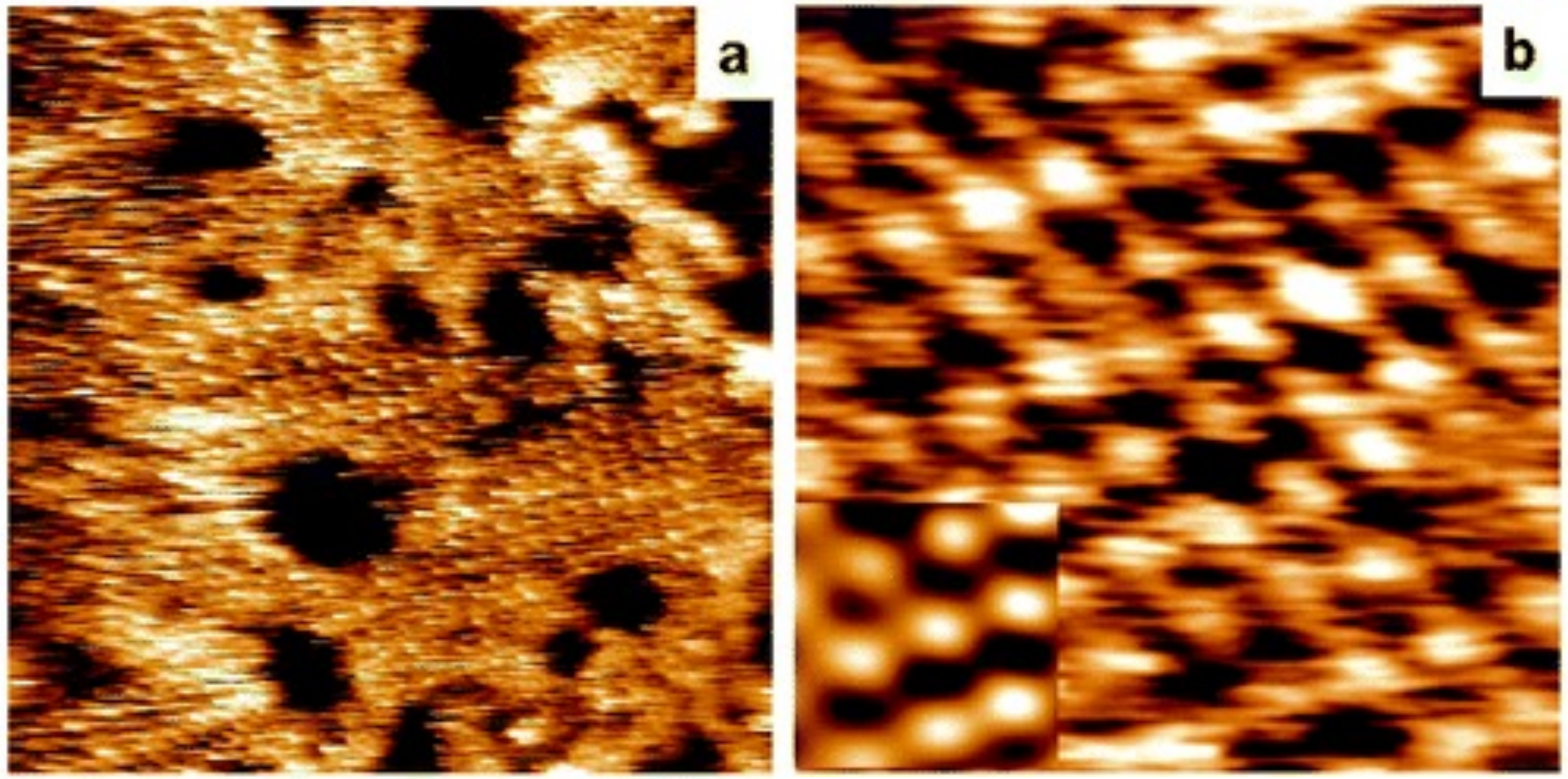




Interactions between two atoms enable measurements of nanomechanical properties

Comparing AFM *vs.* STM – Hexadecanethiol (C16) on Au (111)





30 nm

4 nm

AFM	STM
Simpler – works in air and liquids	More complex (requires UHV and low temp.)
Conducting/non-conducting surfaces	Only conducting surfaces
0.1-10 nm (0.1 is ultimate best equipment)	0.1 nm (0.01 nm in vertical direction)
Topography, **force measurements, mechanical properties**	Topography, electronic properties
Uddin *et al.* | *Res. Phys.* | 2017	Mendoza *et al.* | *Langmuir* | 2006

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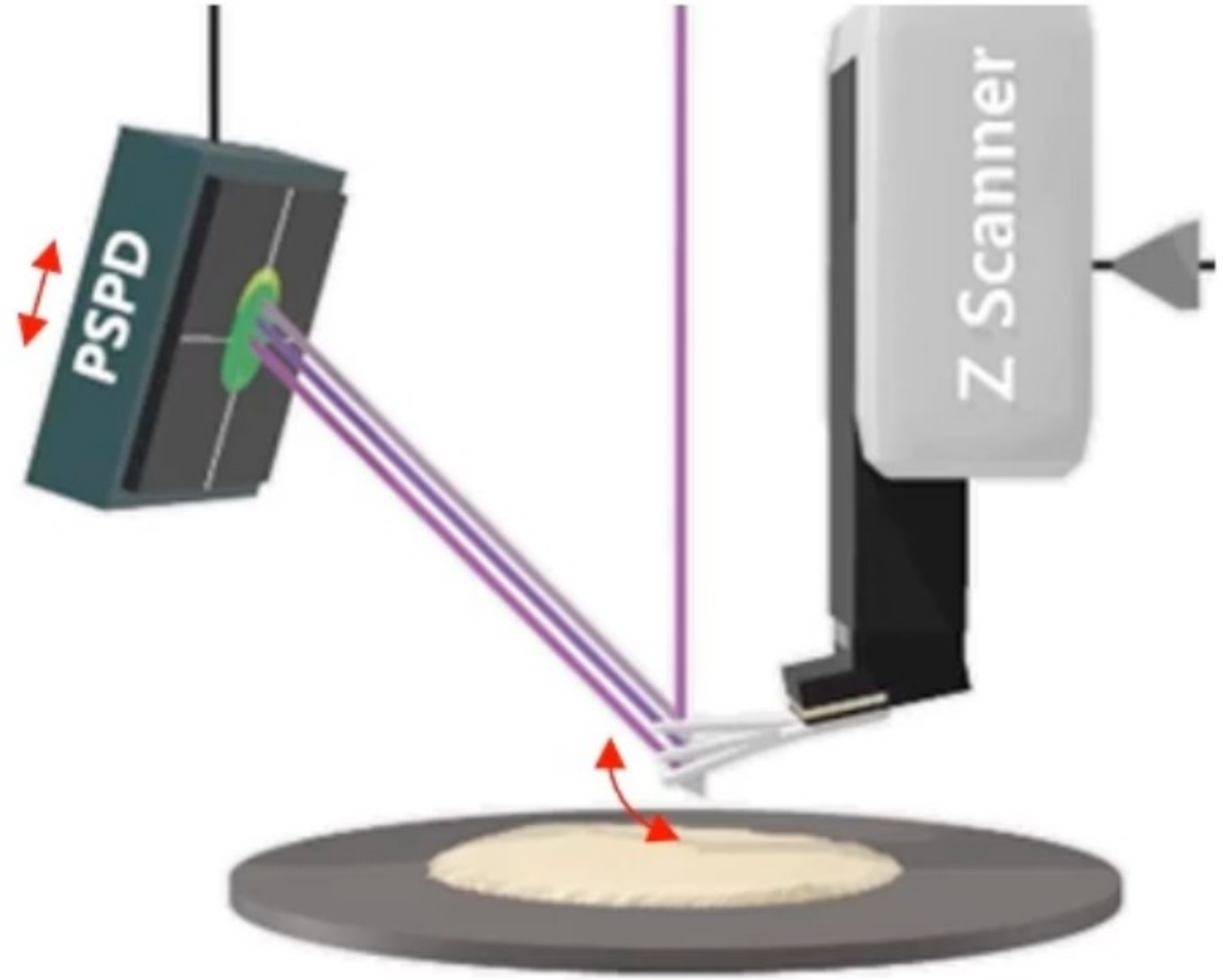
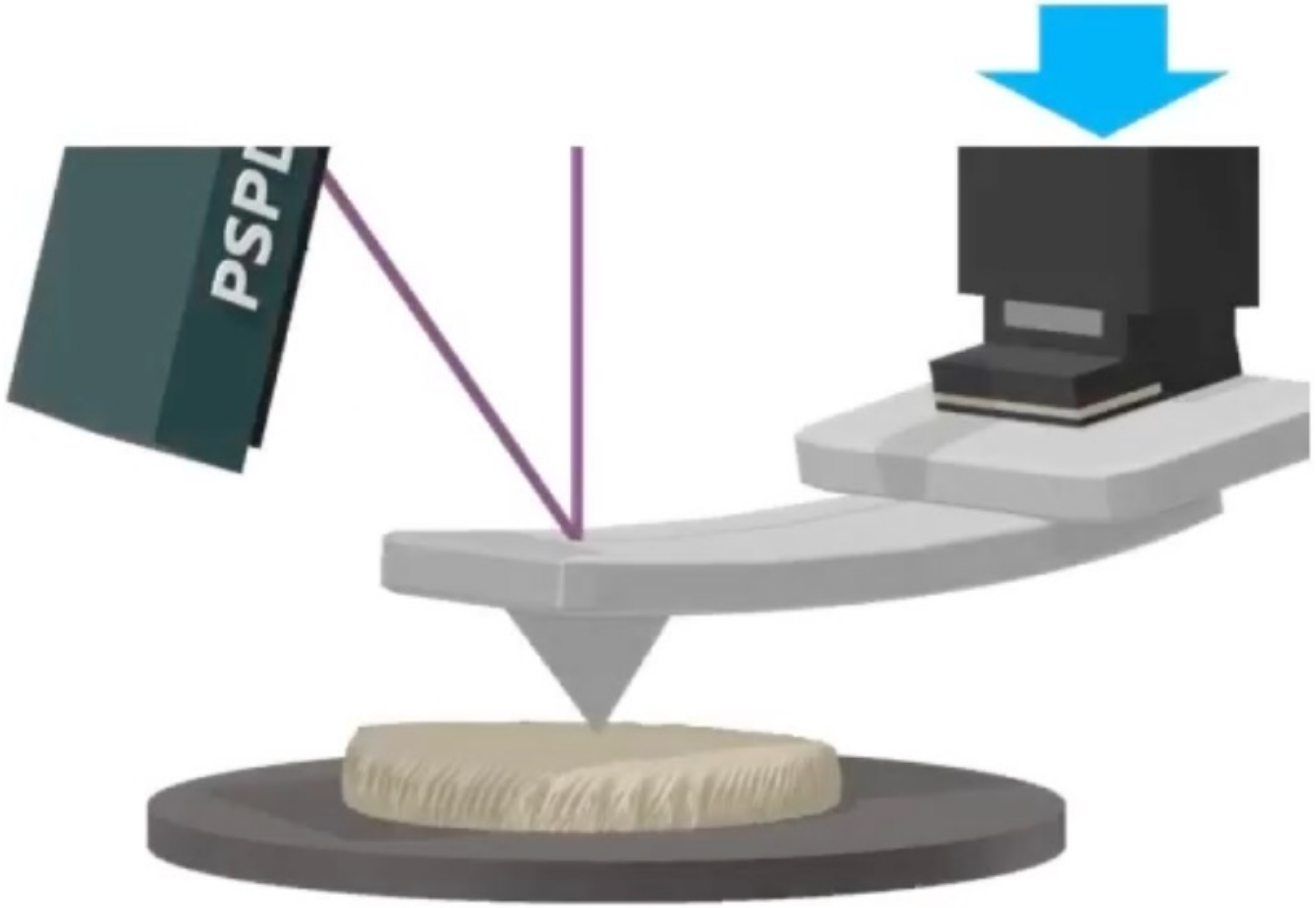
Atomic Force Microscopy (AFM): From Images to Interactions

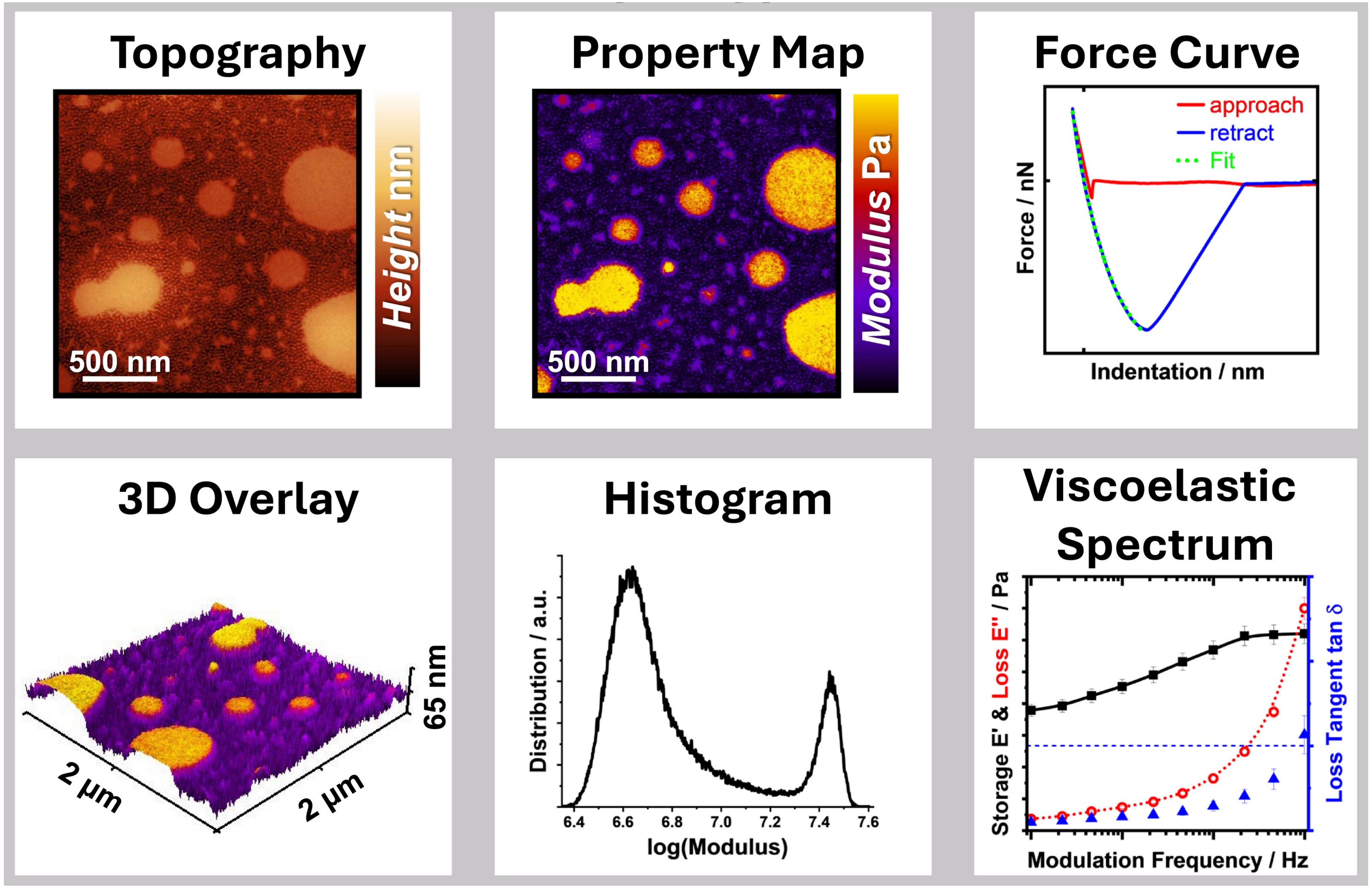


Surface Imaging
Height information



Mechanical properties
Force spectroscopy

Measuring Force/Mechanical Properties of Surfaces



Kim *et al.* | *STAR Protocols* | 2025

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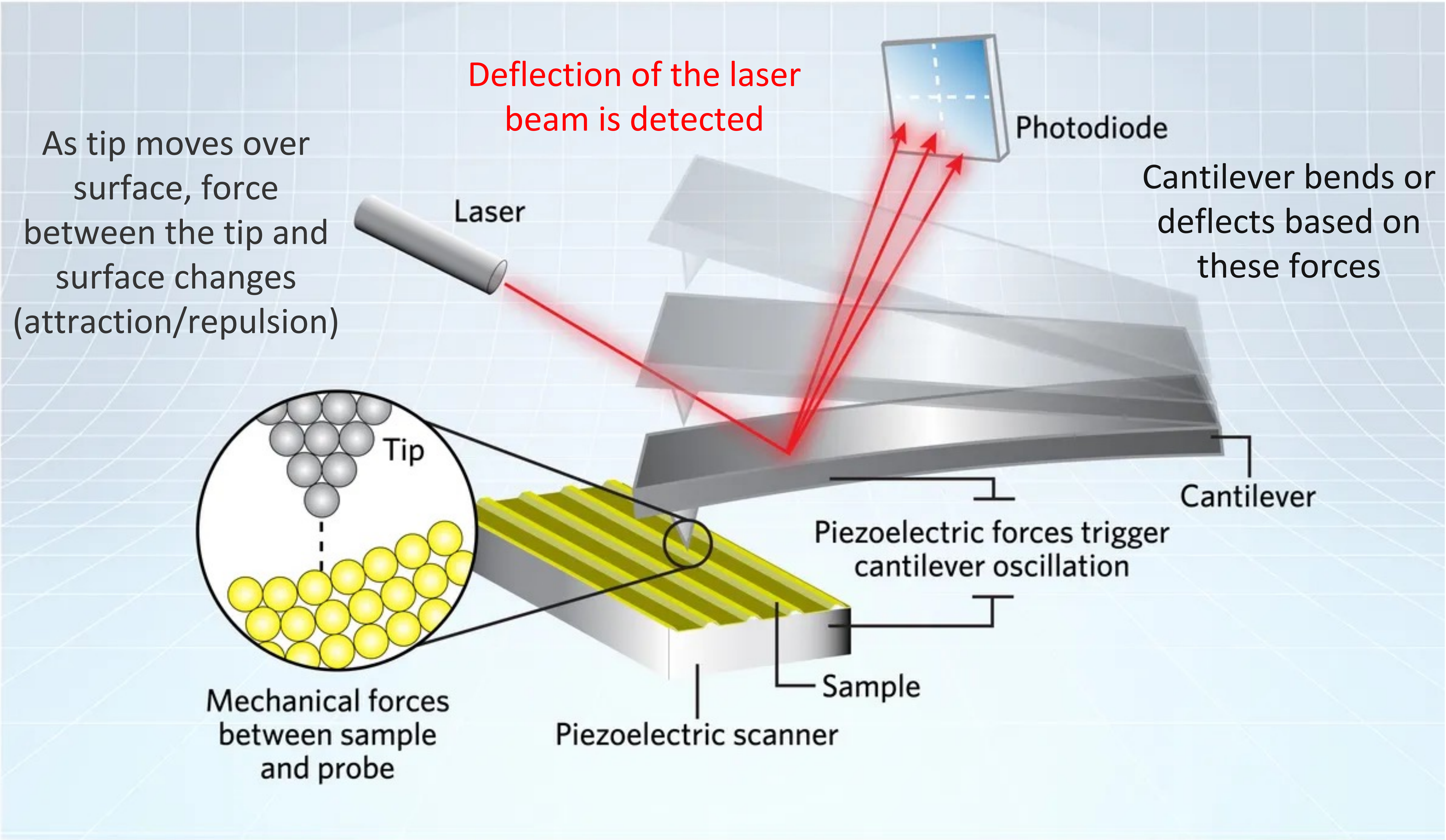
How Can We “See” What is Happening on Surfaces?

Atomic Force Microscopy (AFM)



TheScientist

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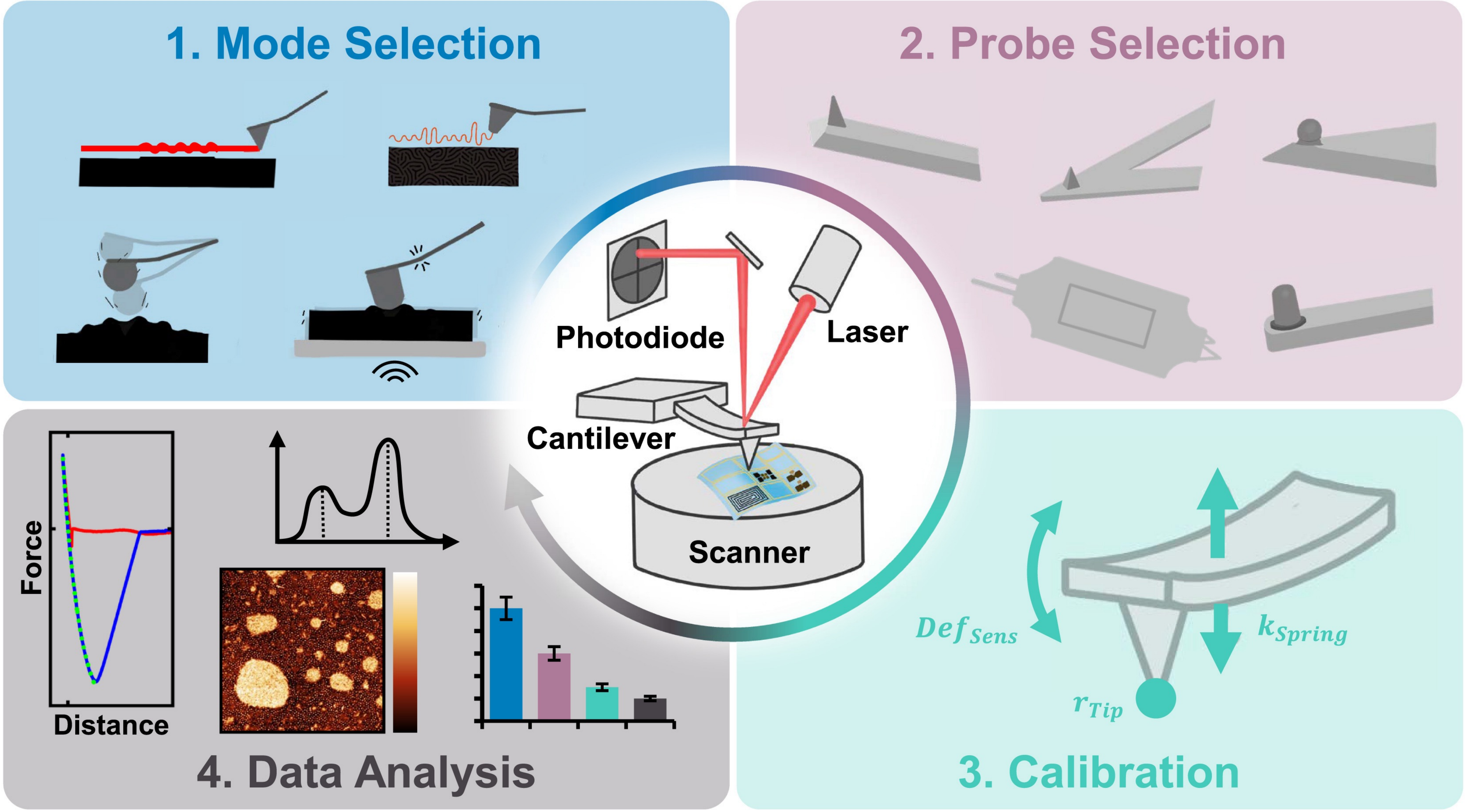
Nanomechanical Characterization of Surfaces



Kim *et al.* | *STAR Protocols* | 2025

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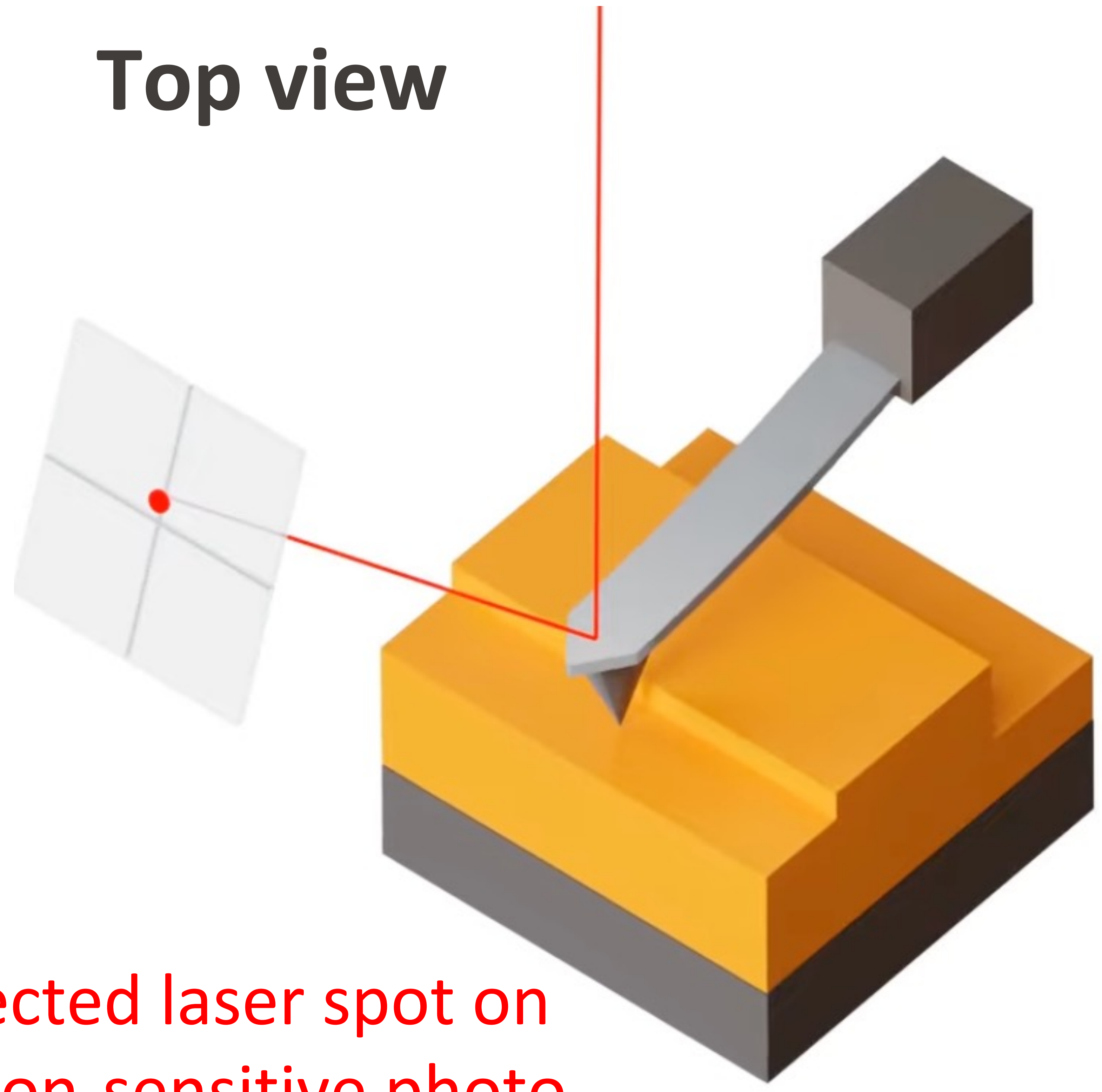
Contact Mode is the Most Basic Mode of AFM for Topography

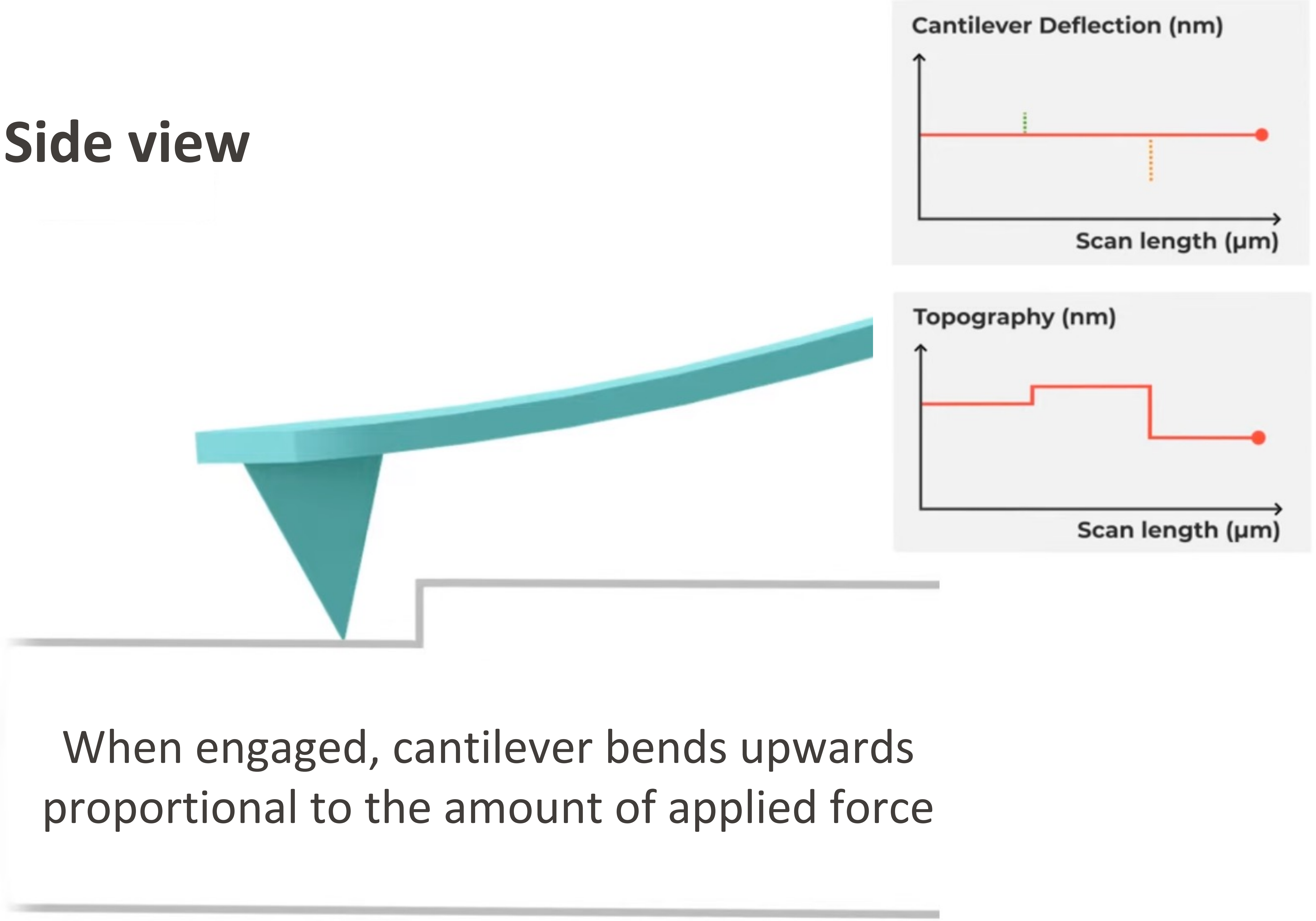
Cantilever scans while applying constant force onto surface of the sample

Top view



Deflected laser spot on position-sensitive photo detector moves due to change in contact force

Side view



When engaged, cantilever bends upwards proportional to the amount of applied force

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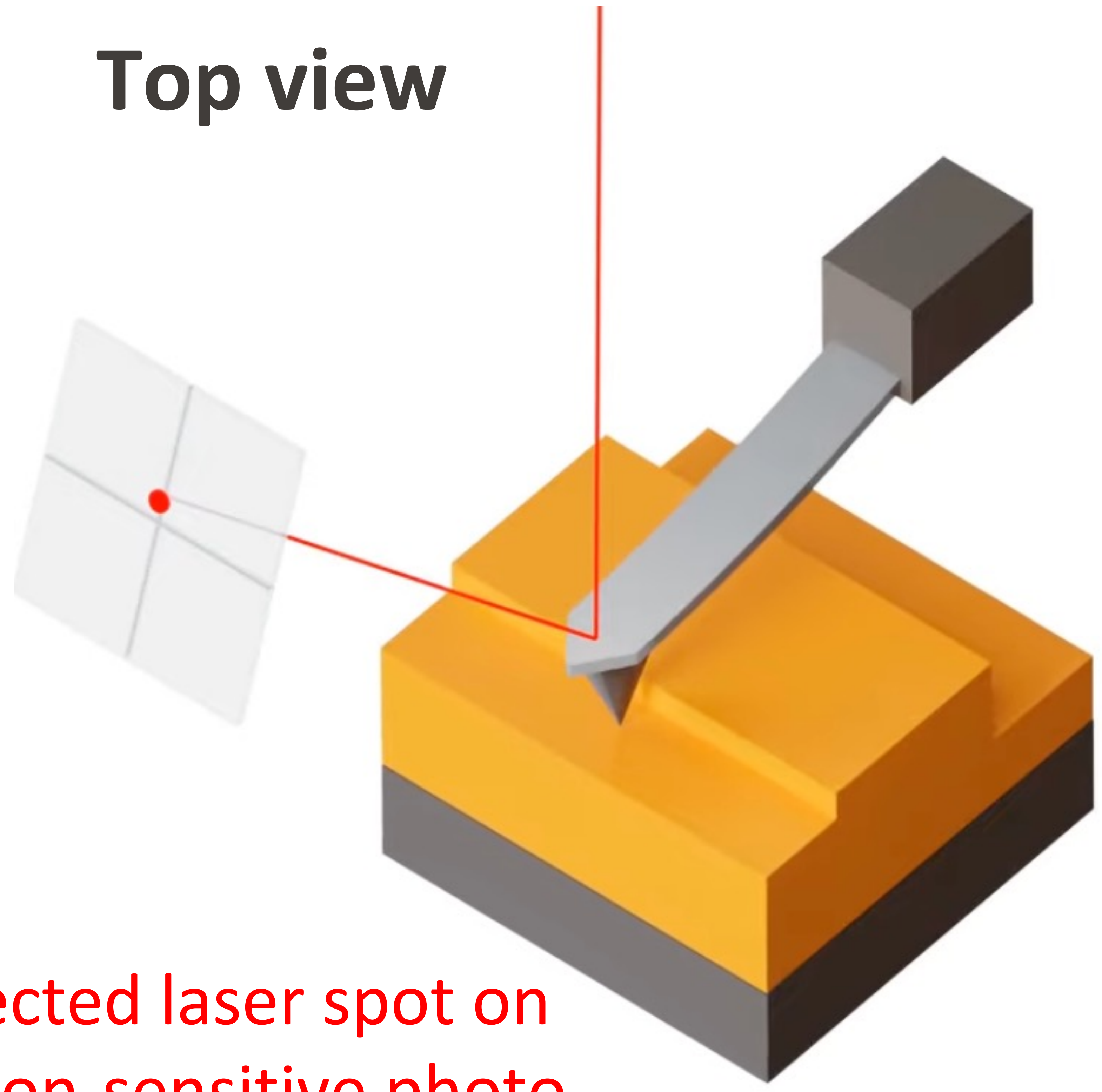
Contact Mode is the Most Basic Mode of AFM for Topography

Cantilever scans while applying constant force onto surface of the sample



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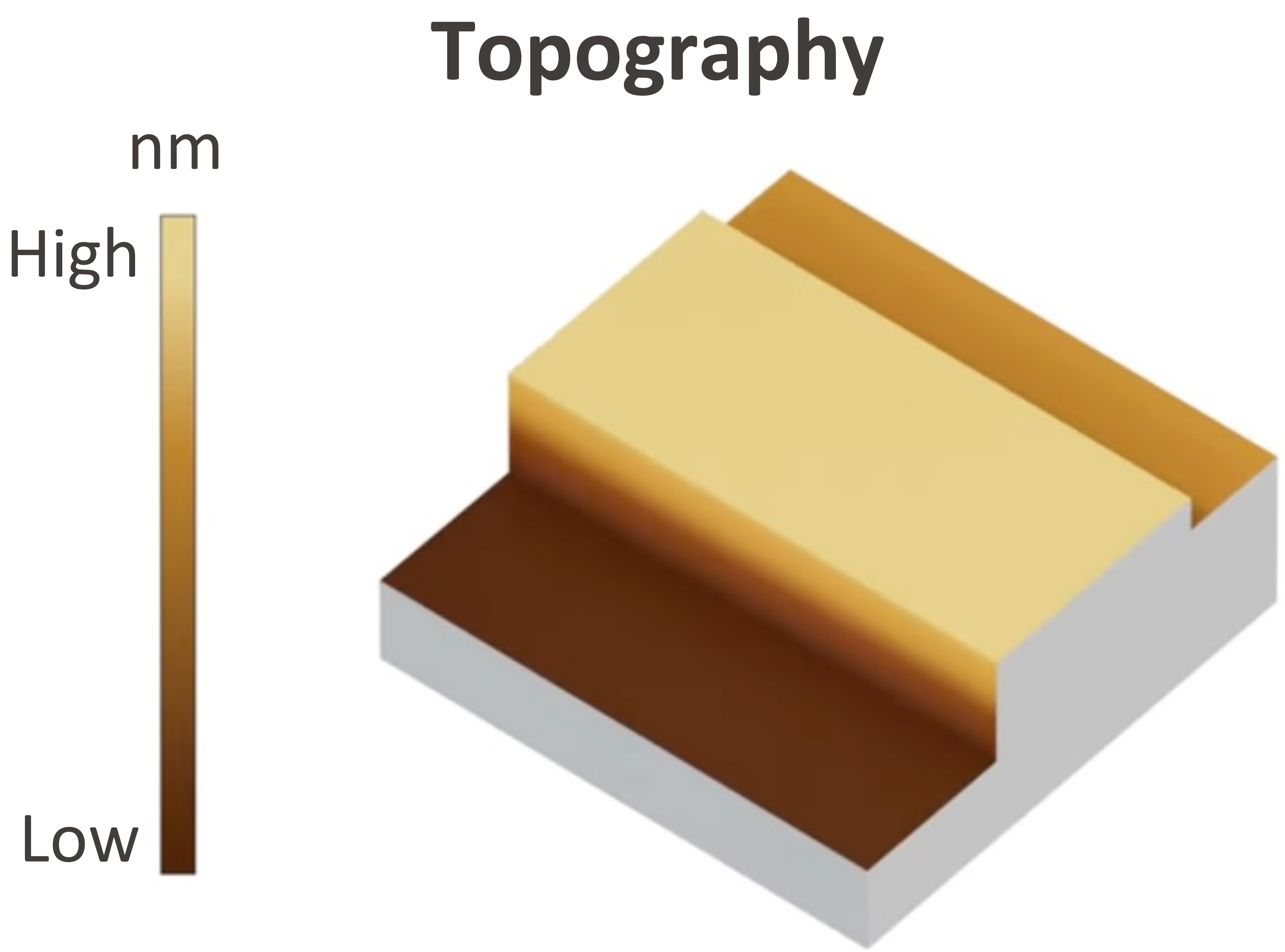
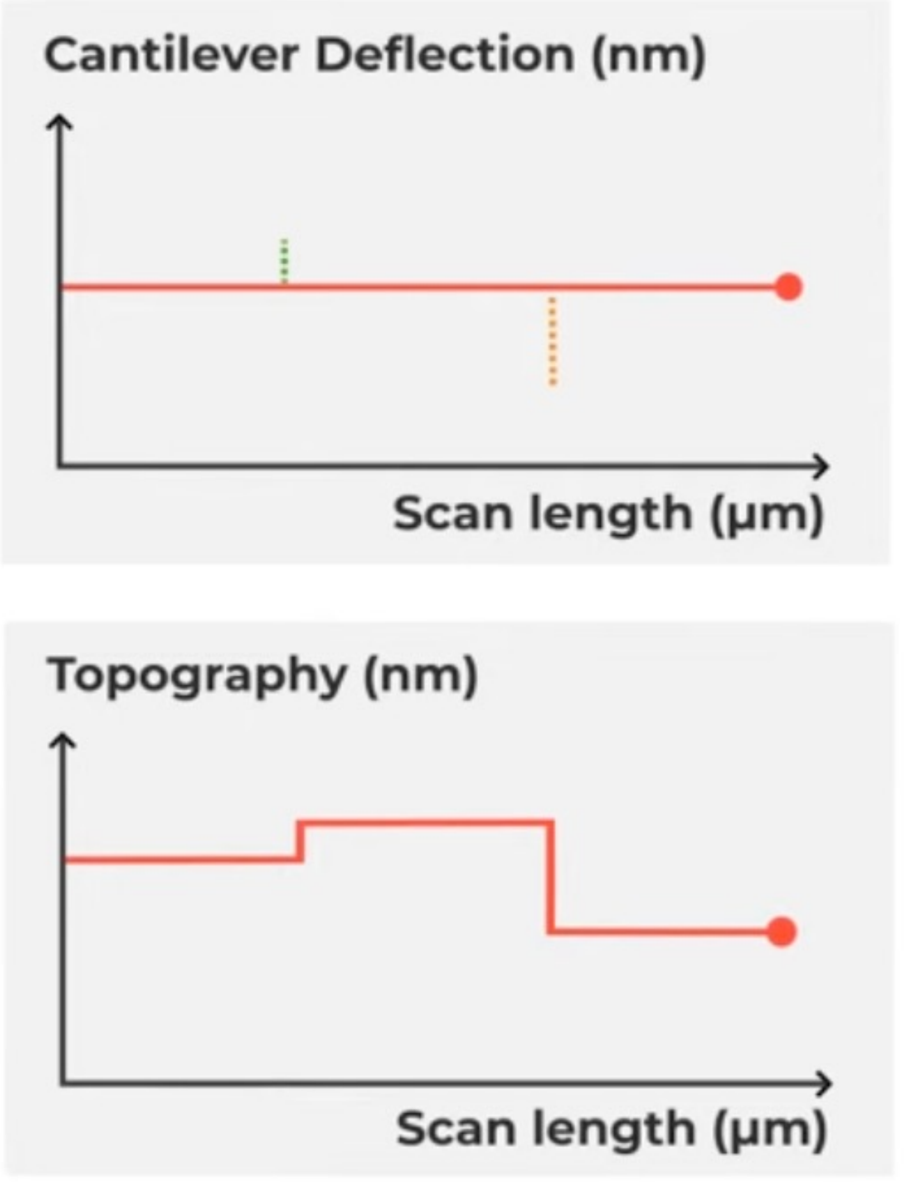
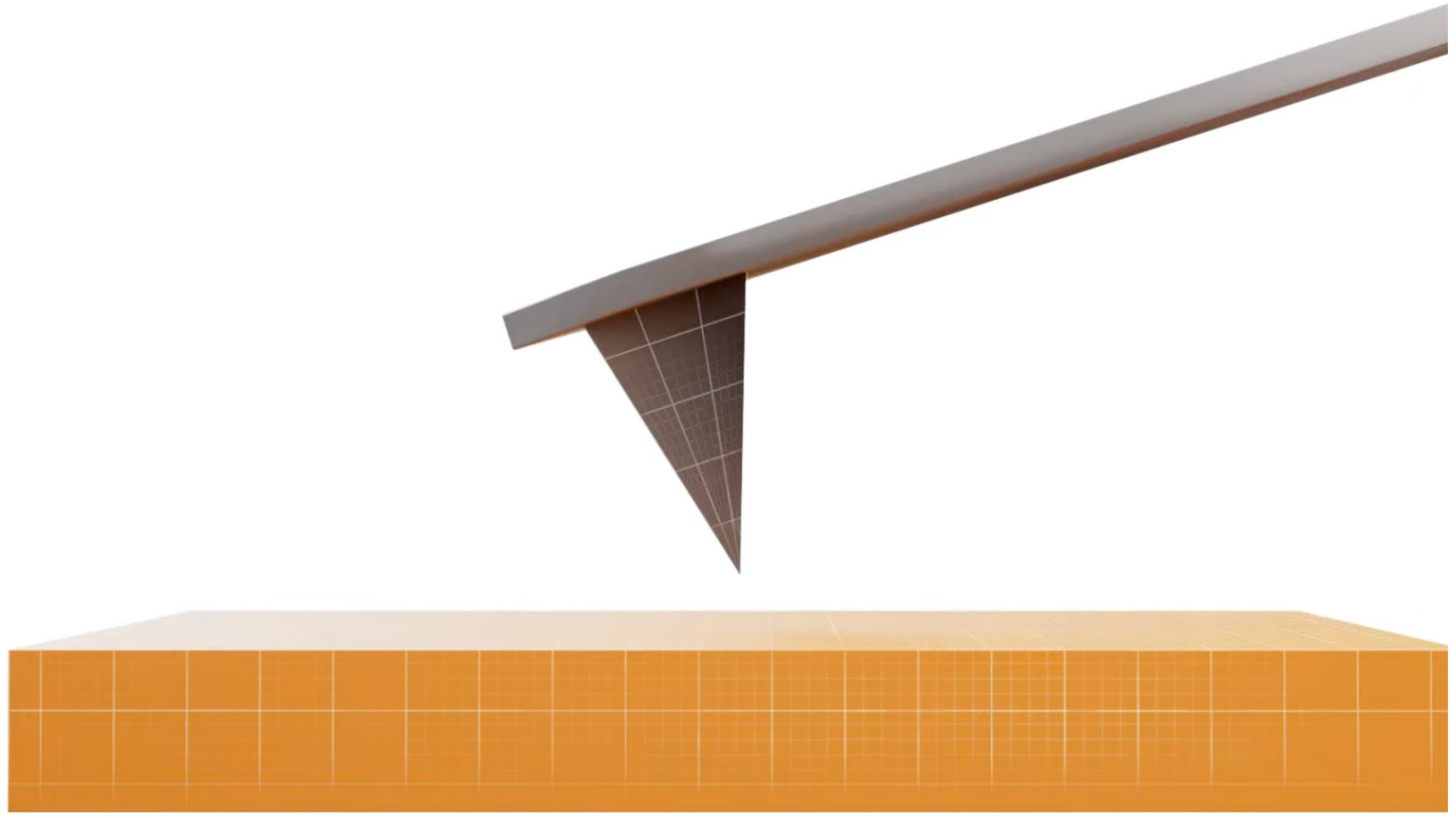




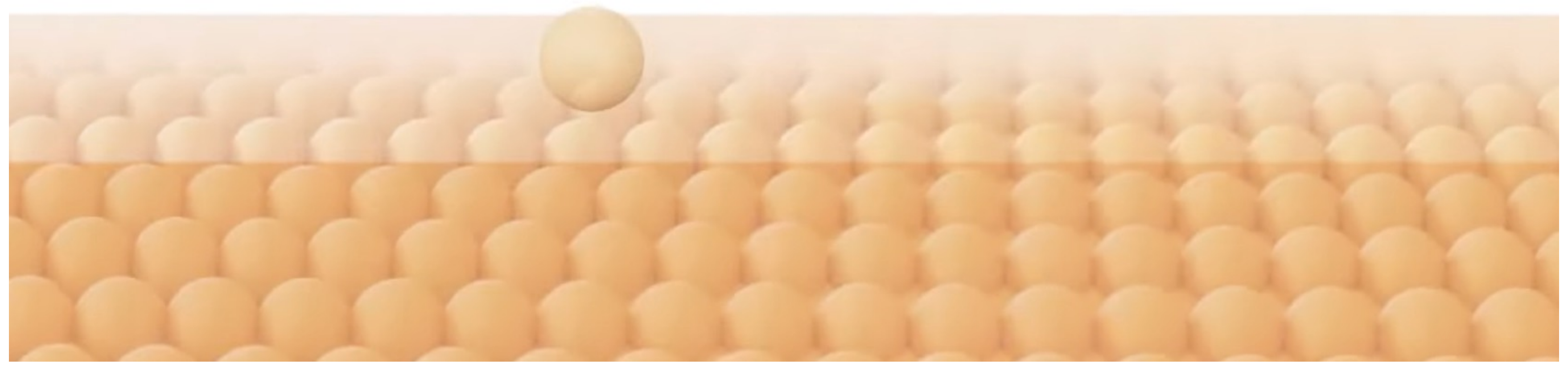
By tracking displacement of the z-scanner obtain the surface topography of the sample

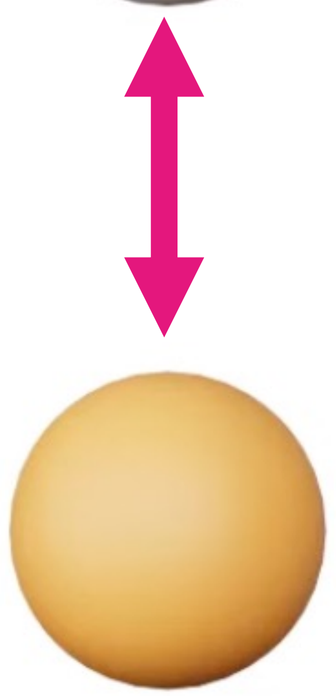
Non-Contact Mode is the Safer Measurement Method

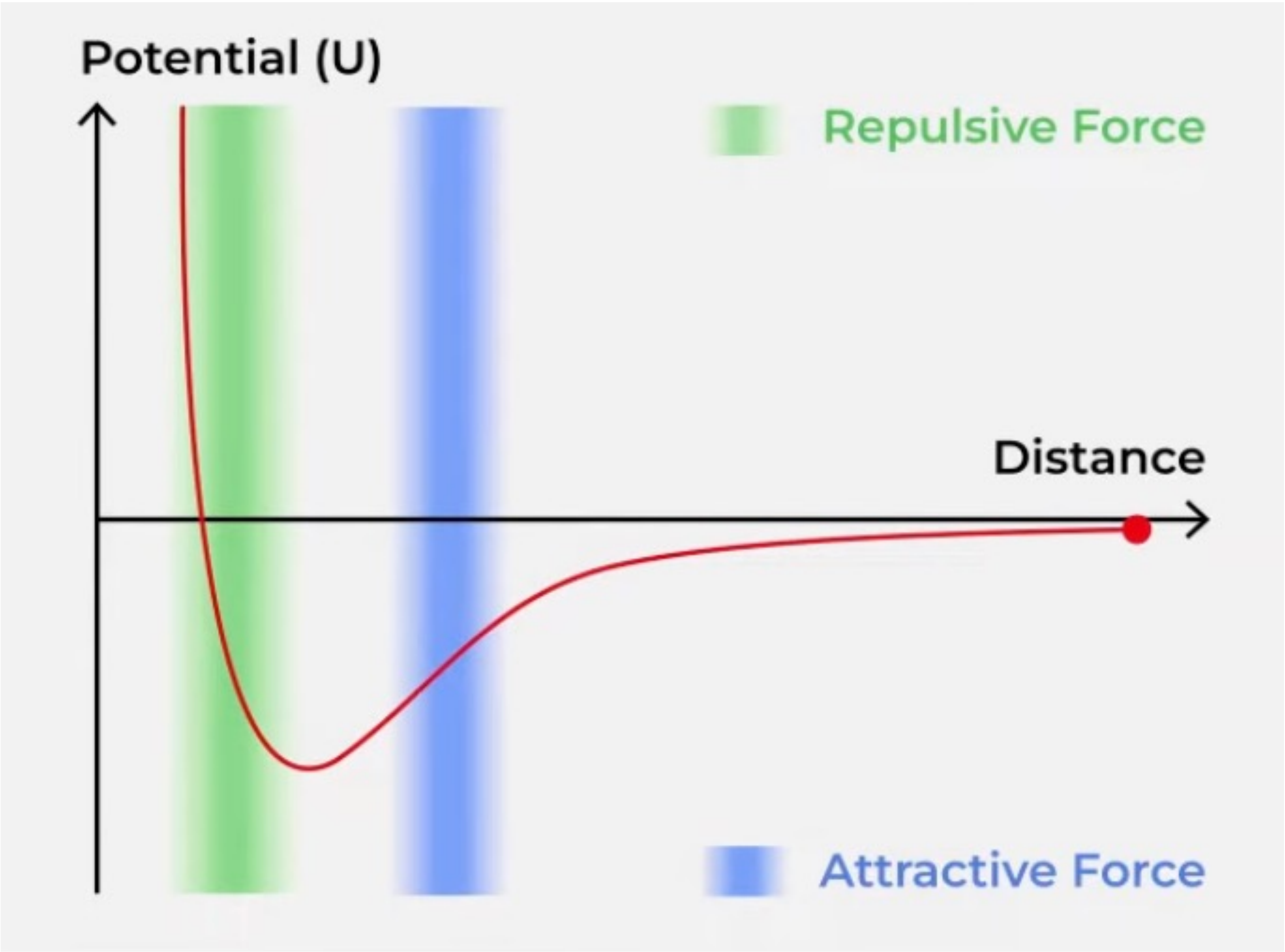
Cantilever does not touch the surface – avoids damage to both the tip and sample



As atoms on tip approach atoms on sample, force arises that pull them closer

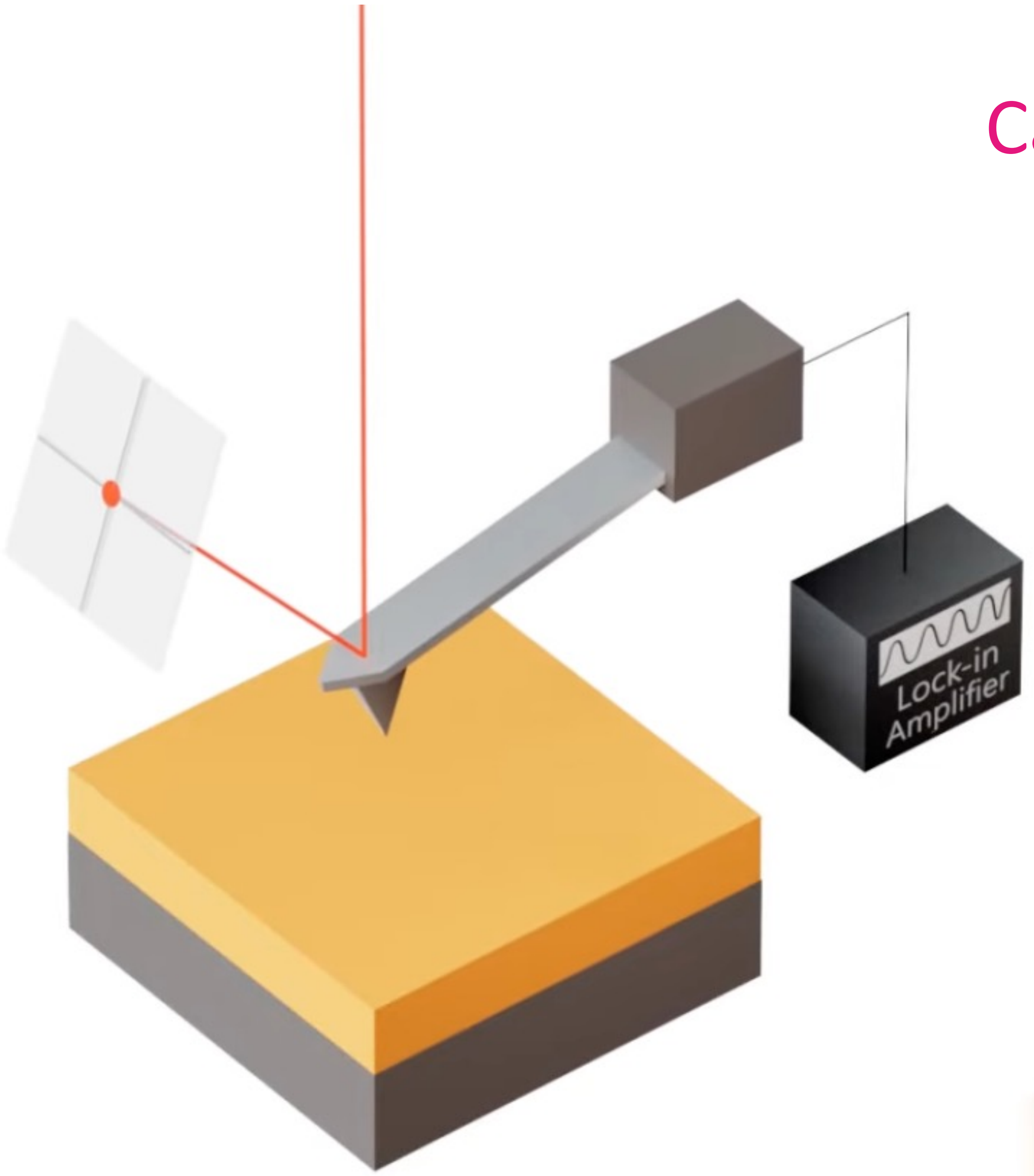




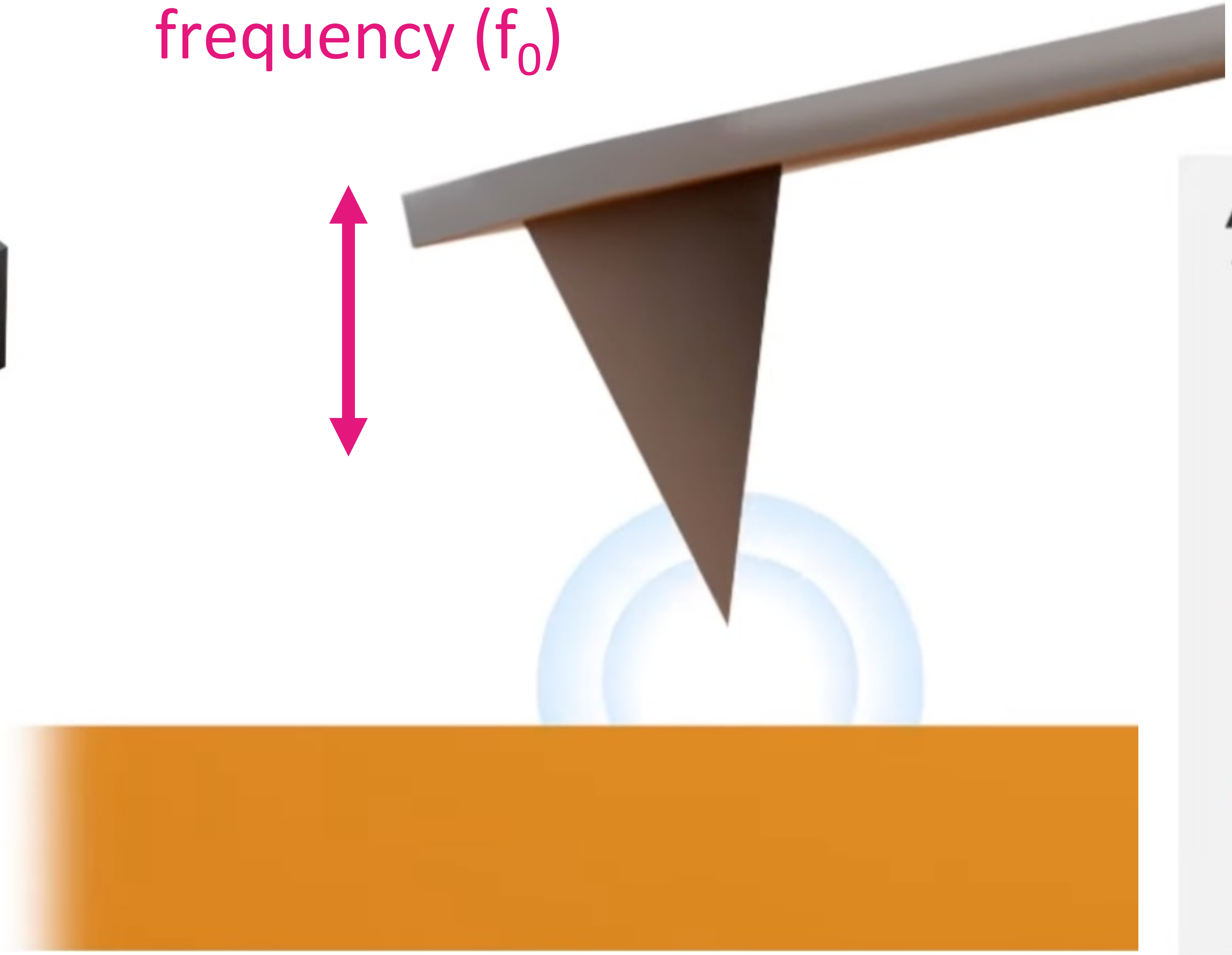


Non-Contact Mode is the Safer Measurement Method

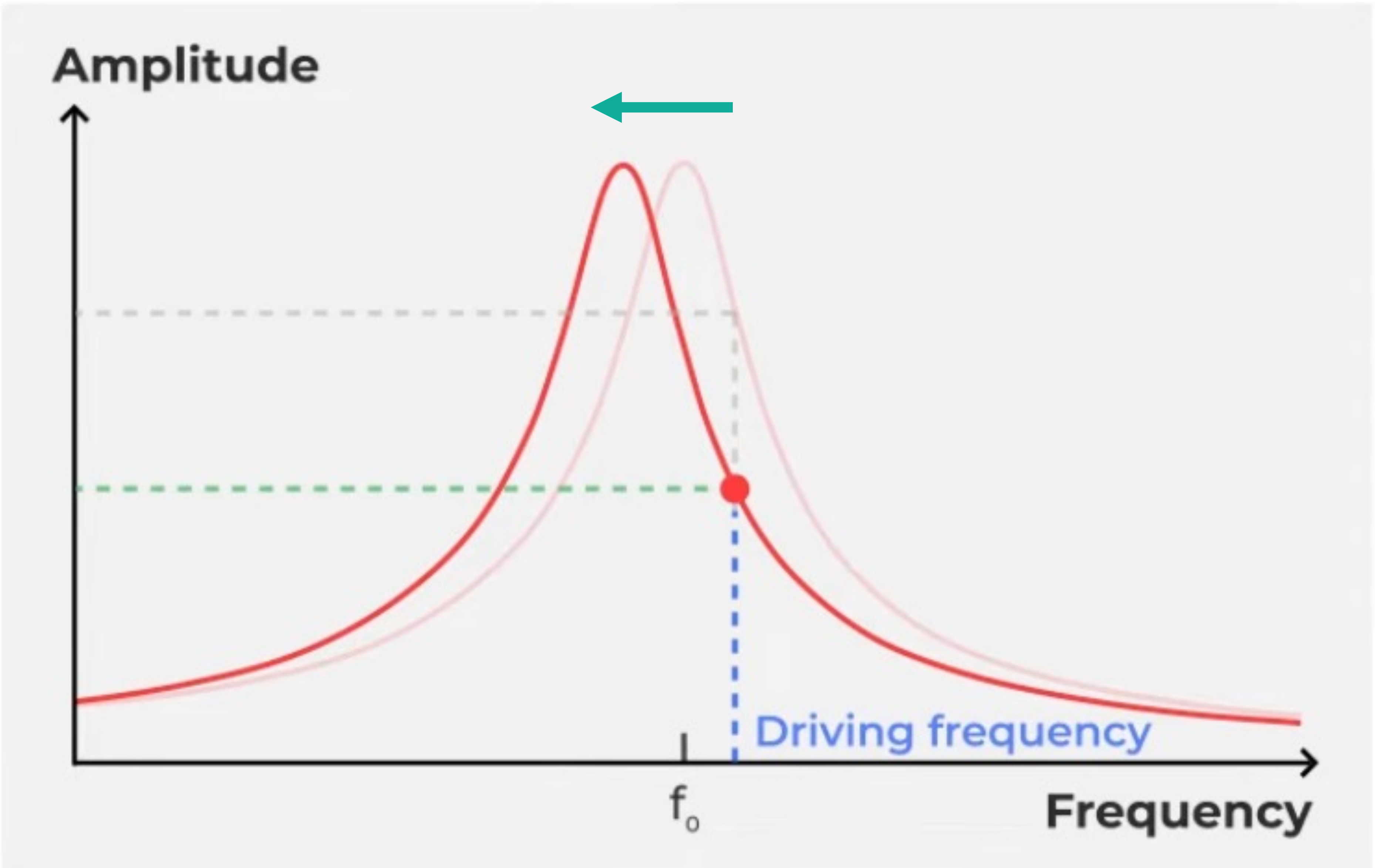
When tip and sample in close proximity, attractive force may not be sufficient to bend the cantilever
➔ resonance frequency of cantilever used to detect subtle force



Cantilever oscillated close to natural resonance frequency (f_0)



When tip gets closer to sample, attractive forces increase ➔ causes shift in f_0 to lower values



Non-Contact Mode is the Safer Measurement Method

As tip and sample come closer

↓

attractive forces strengthens

↓

decrease in amplitude of cantilever oscillation

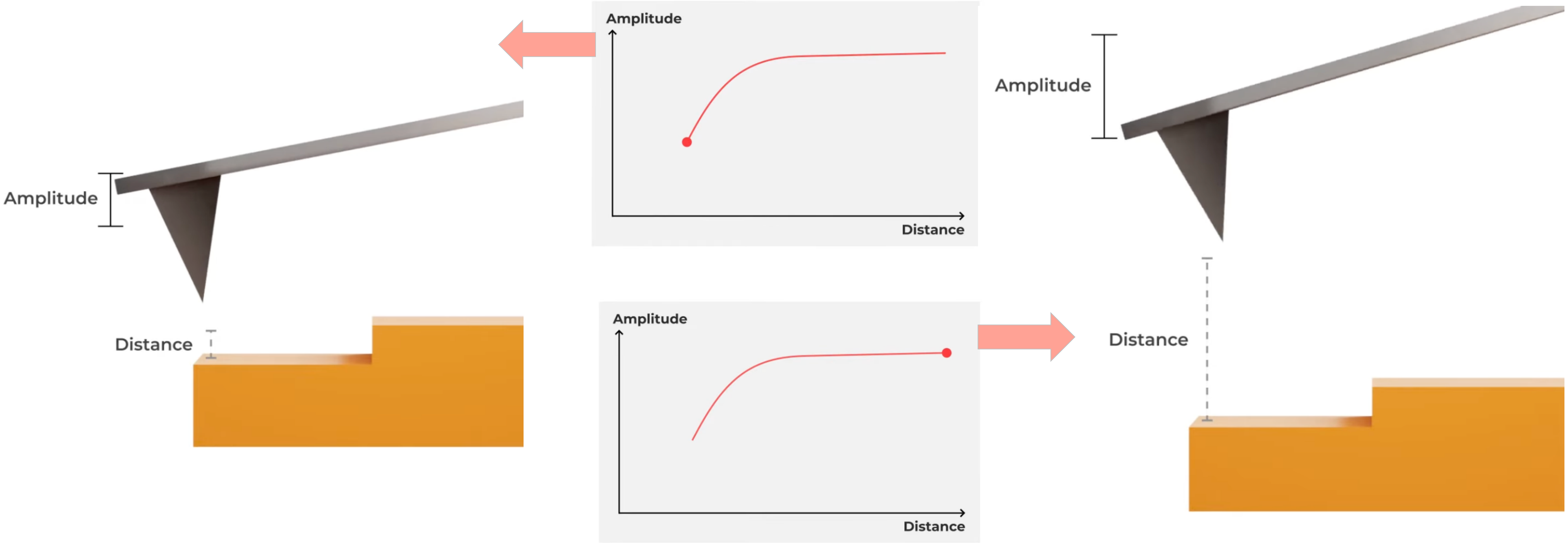
As tip and sample go further apart

↓

attractive forces weaken

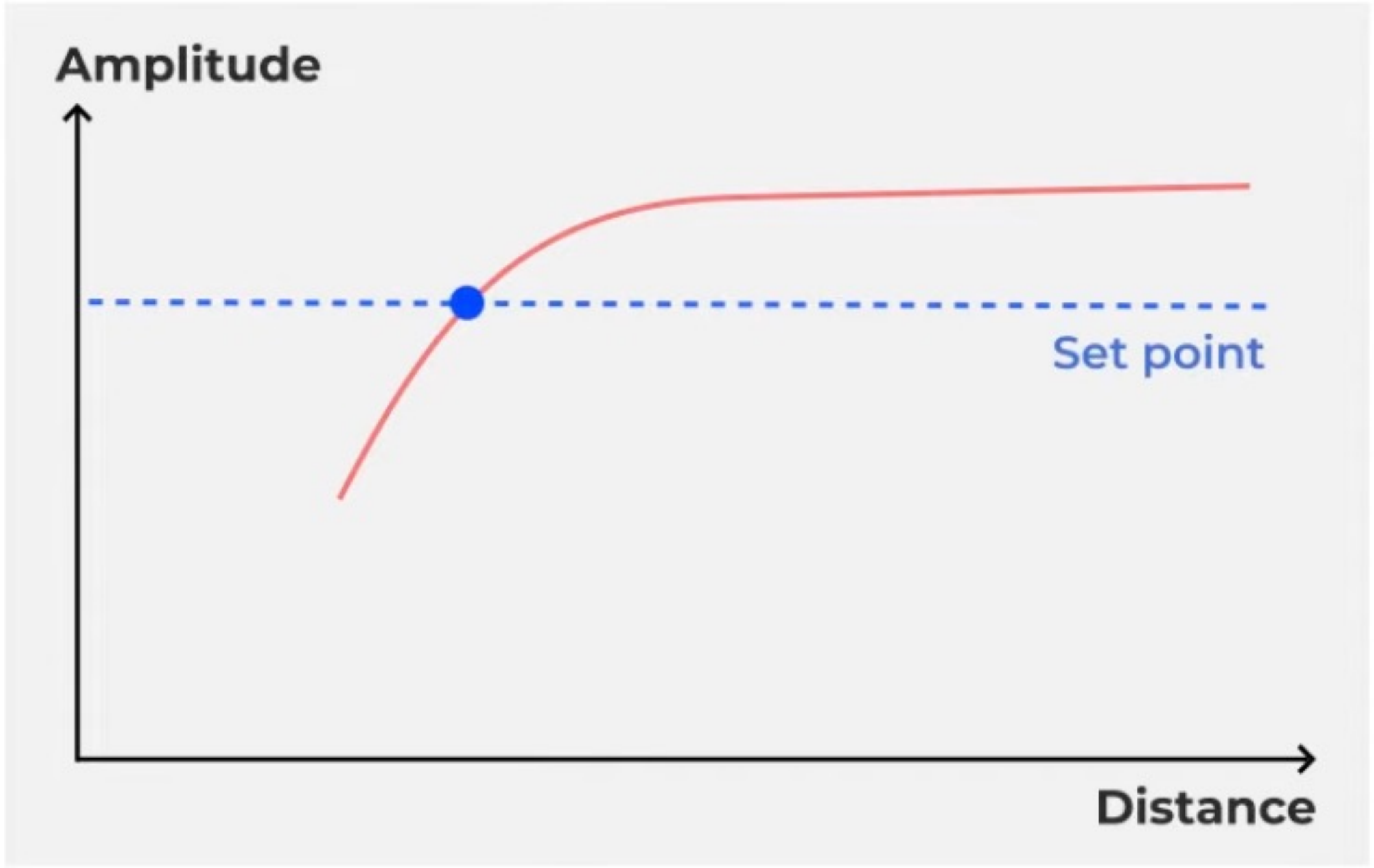
↓

increase in amplitude of cantilever oscillation

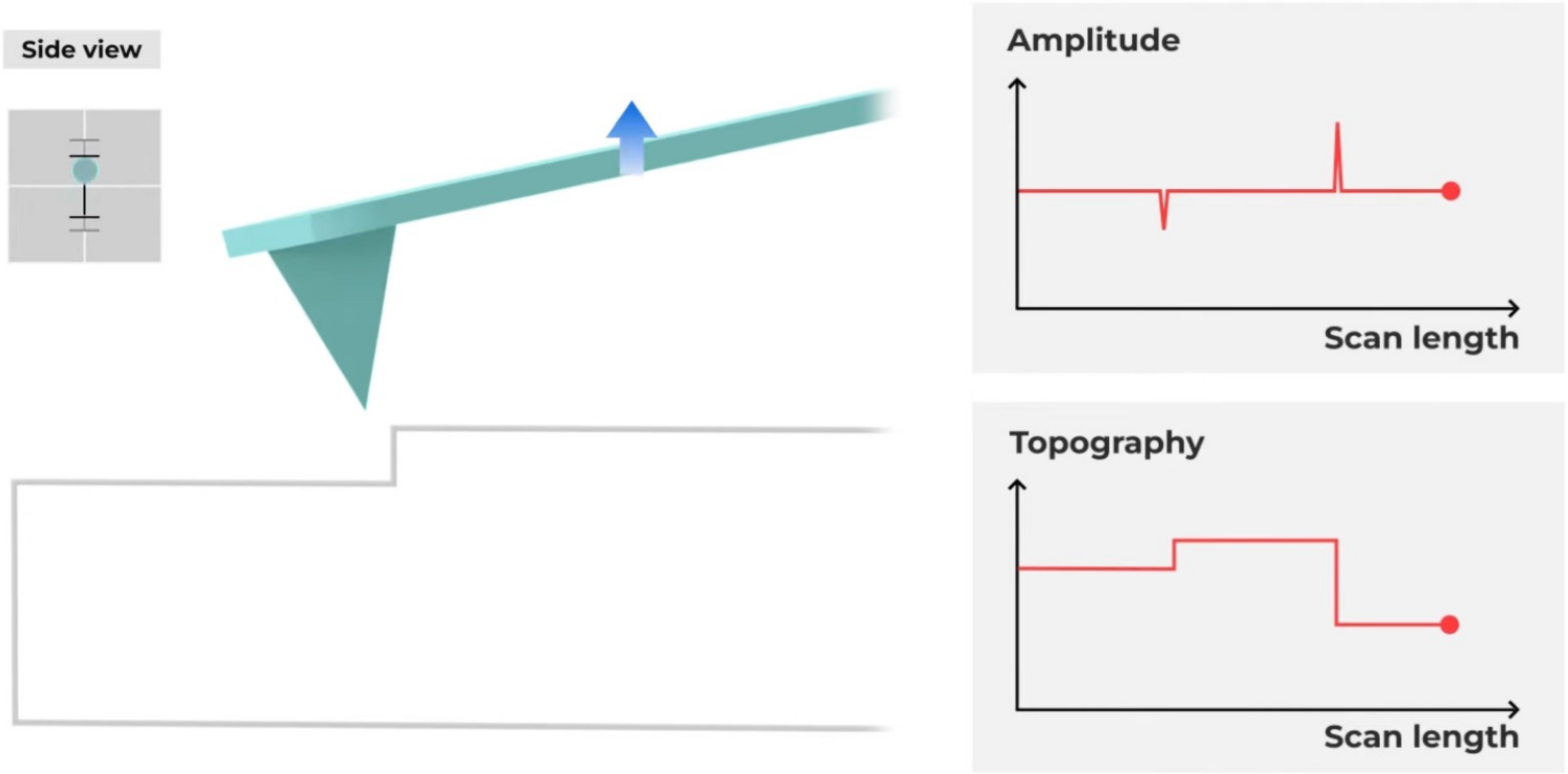


Non-Contact Mode is the Safer Measurement Method

To scan sample, a set point (reference amplitude) is selected for feedback control



During scanning, feedback loop ensures consistent tip-sample distance by adjusting z-scanner height to maintain constant amplitude



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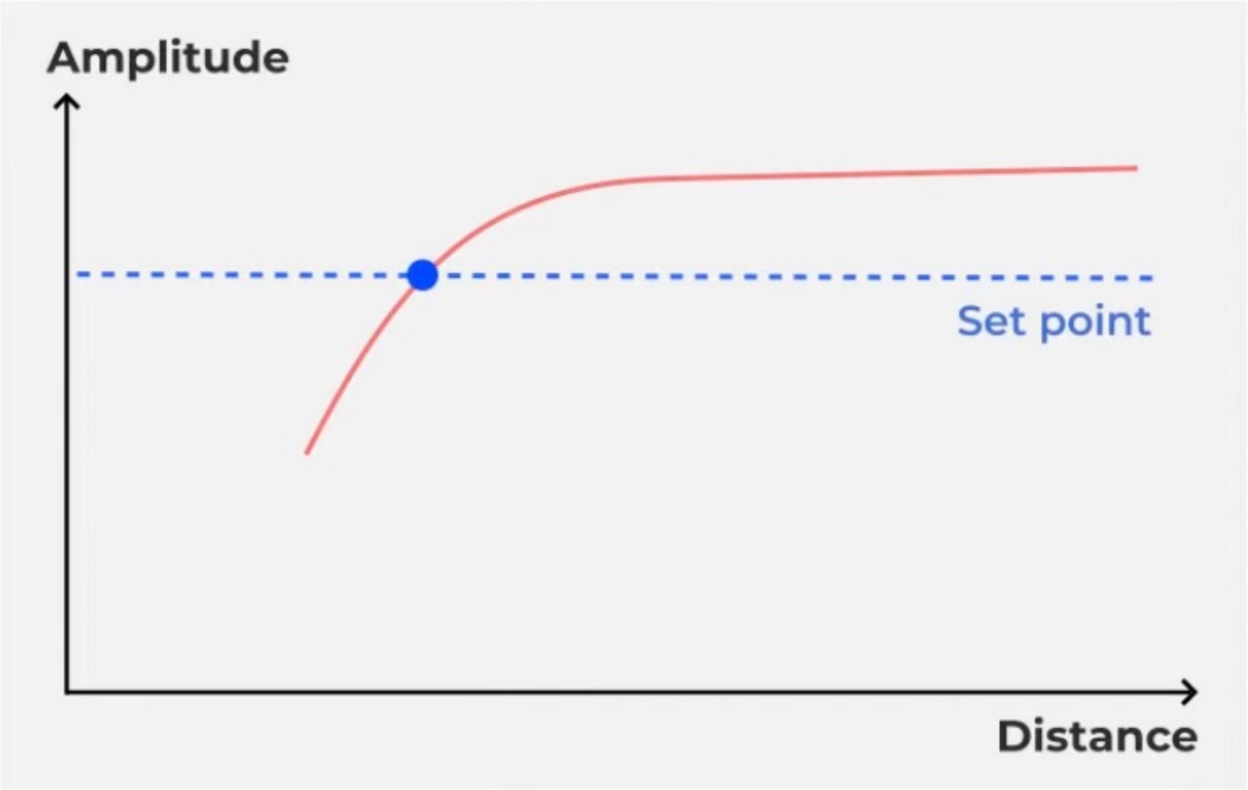
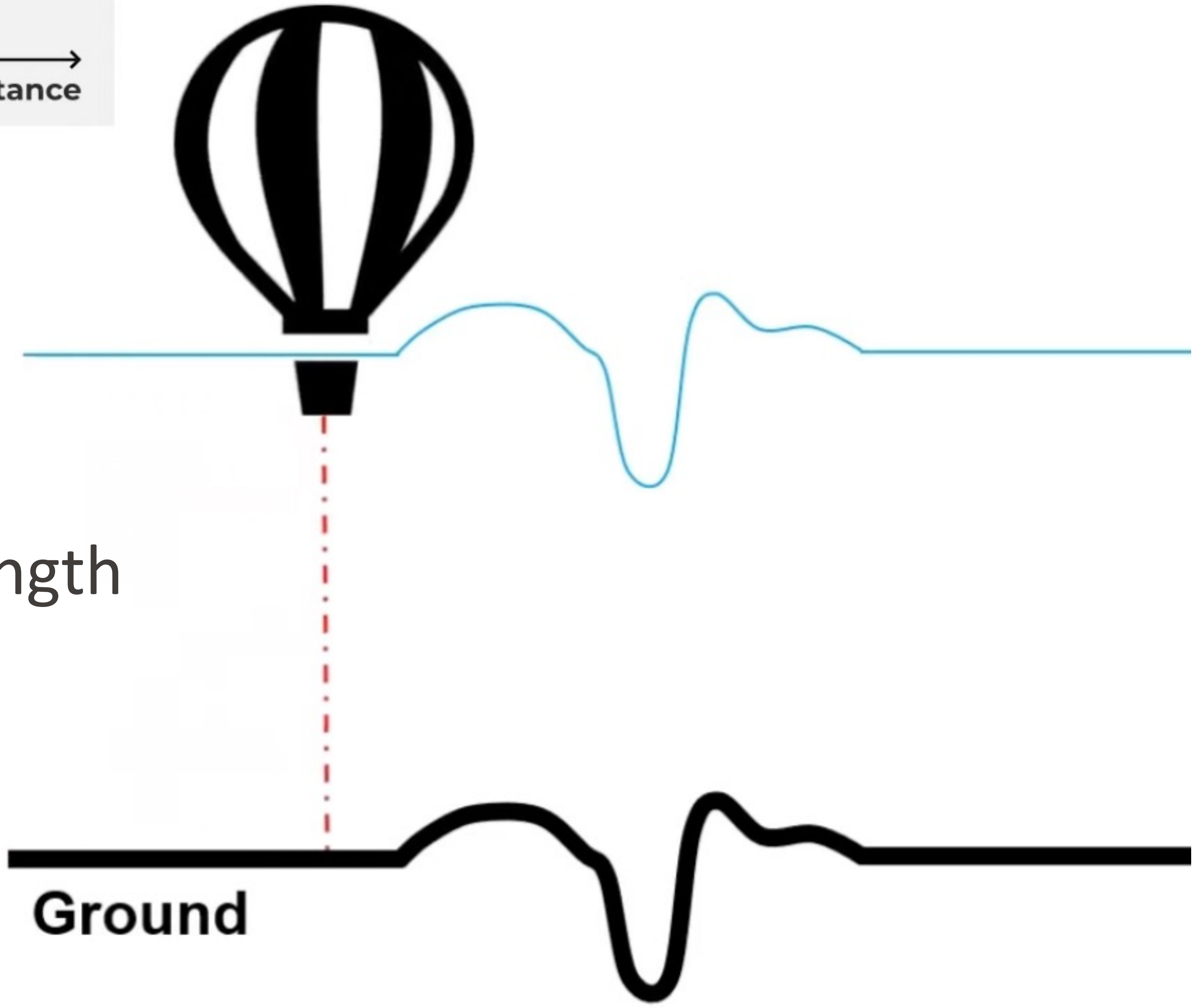
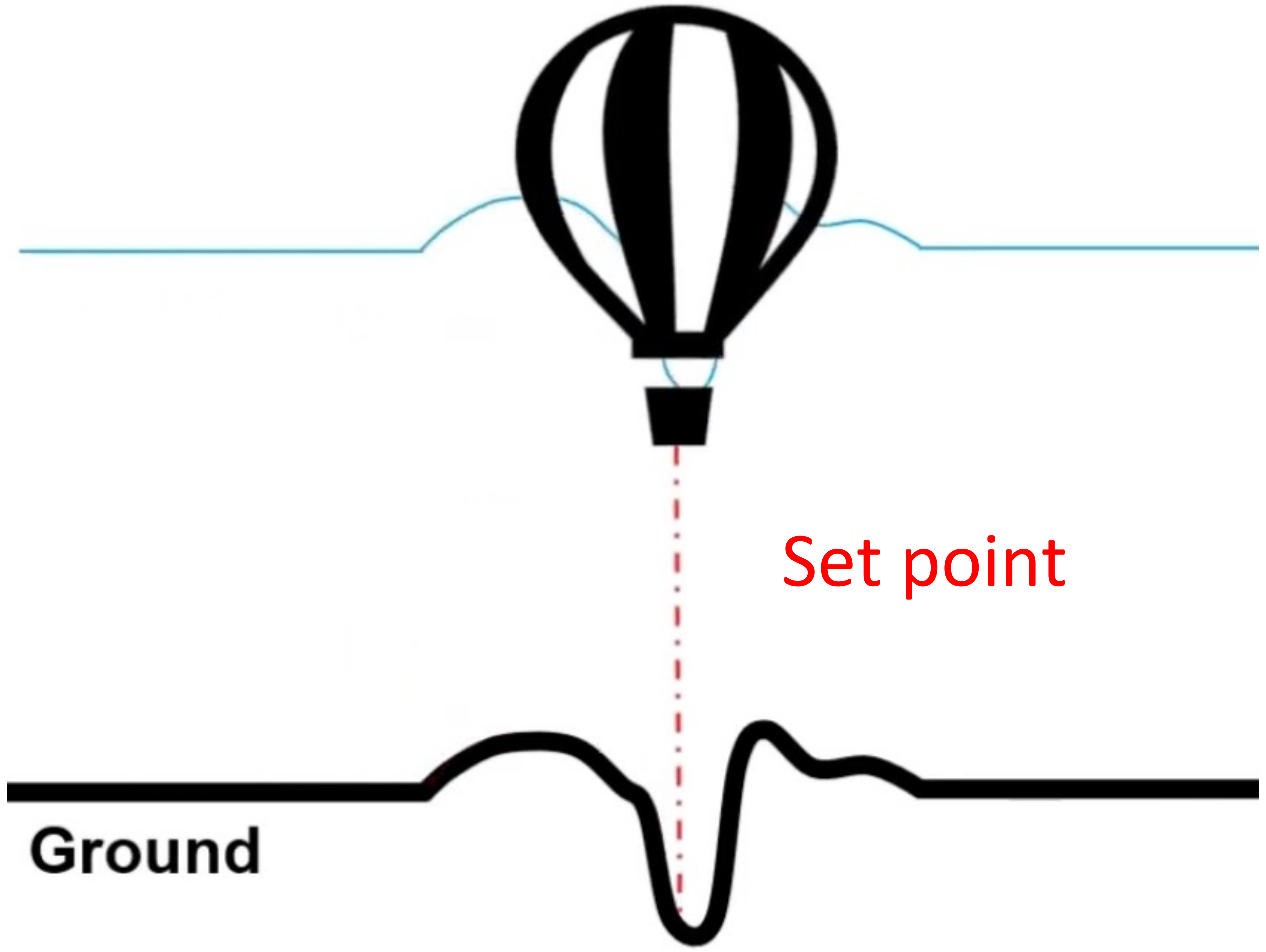
Explaining Set Point From the Perspective of a Hot Air Balloon



Z-scanner of AFM

Fixed focal length camera

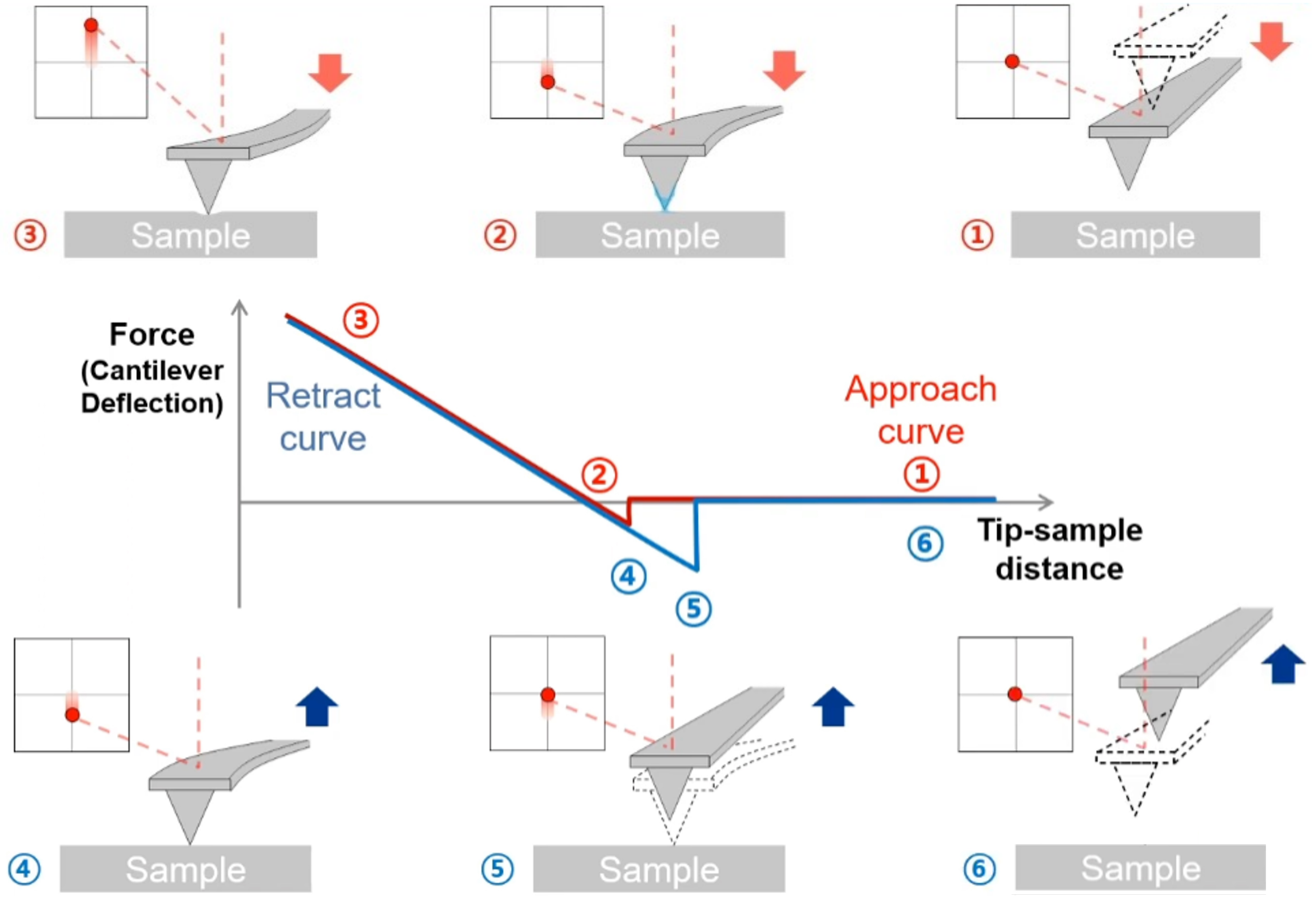




Contact *vs*. Non-Contact Mode AFM

Feature / Aspects	Contact Mode AFM	Non-Contact AFM
Tip–sample interaction	Tip remains in continuous physical contact with surface	Tip oscillates near the surface without touching it (only long-range forces)
Potential for sample / tip damage	High — can deform or scratch soft samples	Low — minimal wear and damage
Image resolution (topography)	Excellent on hard, flat surfaces; can be degraded by tip wear on soft materials	High, but sensitive to contamination and environmental noise
Suitability for soft/biological samples	Poor to fair (risk of damage)	Good if stable in air/vacuum Difficult in liquid
Operation in liquid	Stable	Difficult — oscillation damped by liquid
Quantitative force measurement	Yes — directly from deflection (ideal for force–distance curves, adhesion, stiffness)	Limited – indirect via force gradients
Speed / scan rate	Fast, robust feedback loop	Slow, due to weak signals and delicate tuning
Complexity of setup	Simple — easy to align and tune	Complex — requires stable environment
Typical applications	Hard materials, tribology, friction mapping, force spectroscopy	Delicate surfaces, molecular-scale imaging, surface potential studies

Force-Distance Curve for Mechanical Measurements



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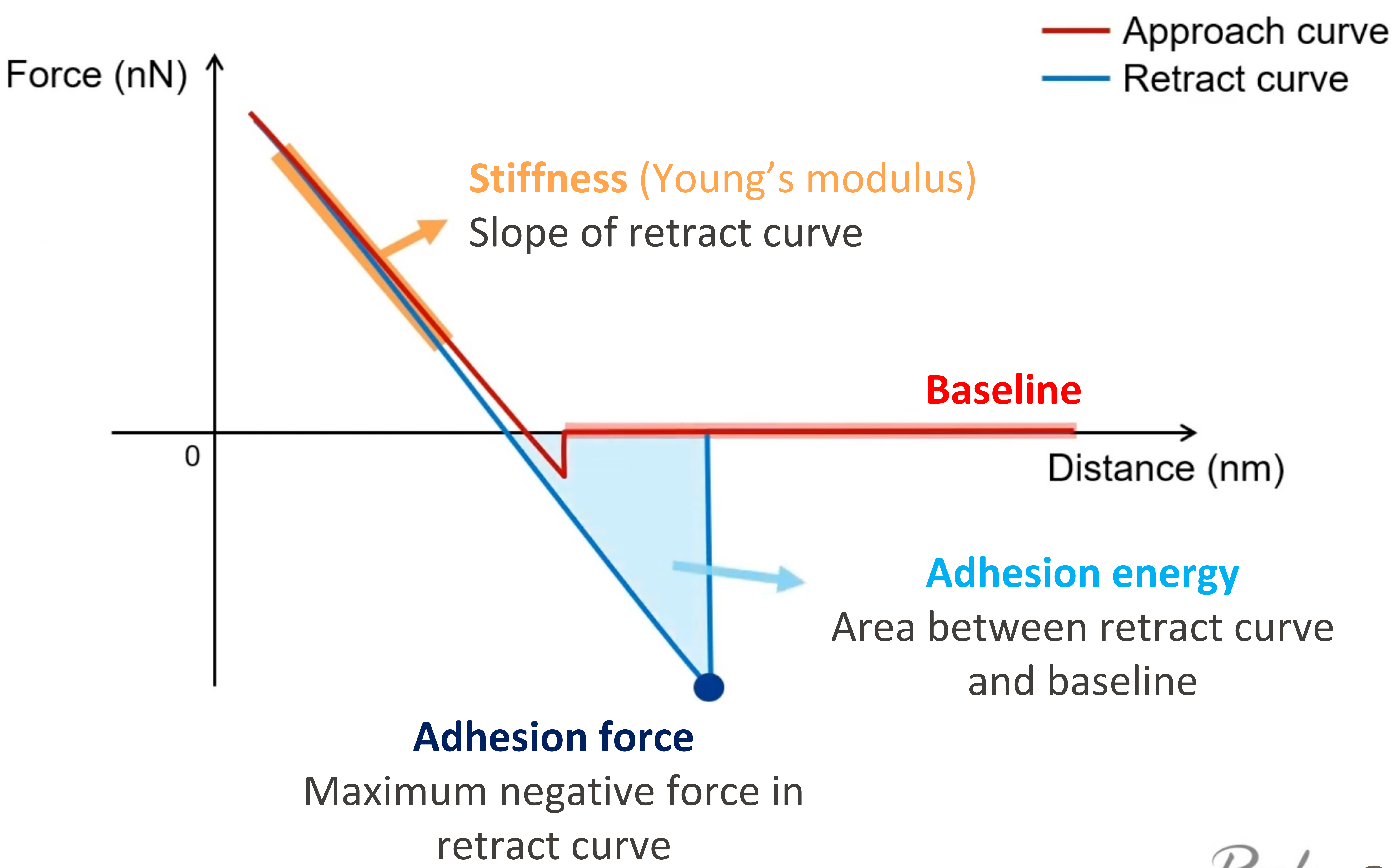
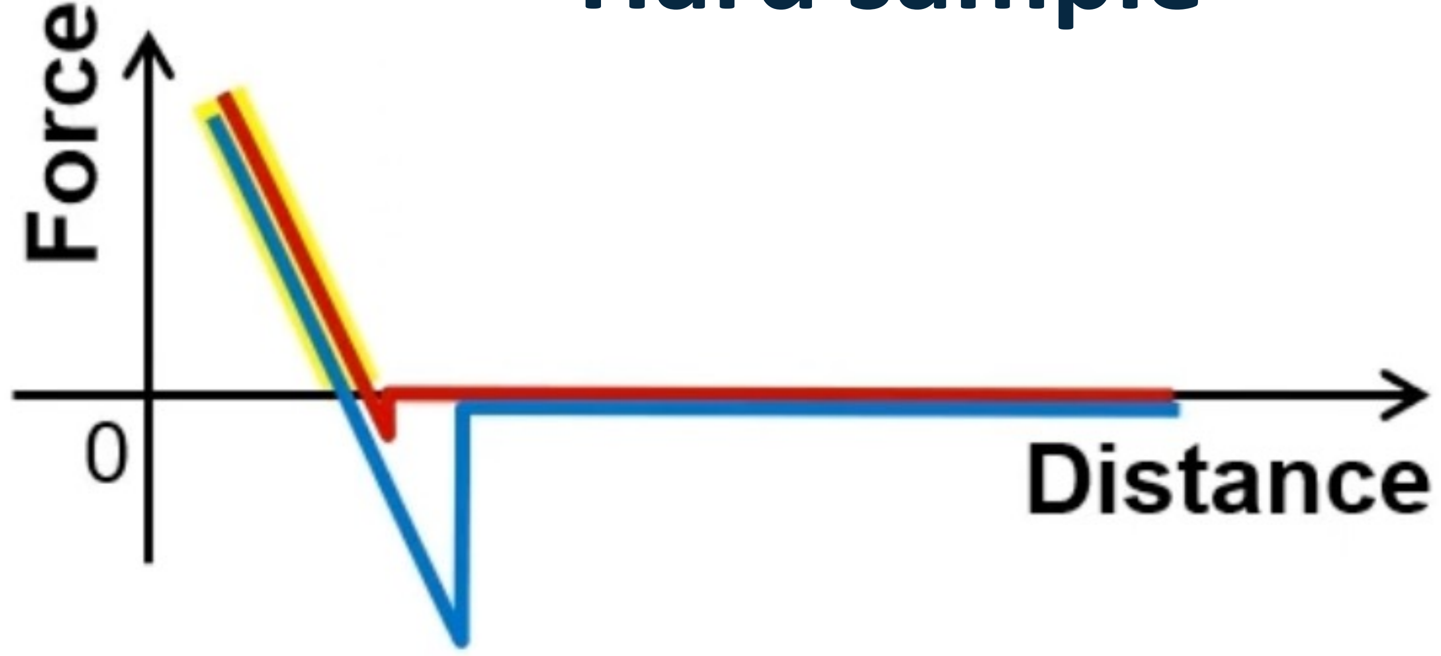
Force-Distance Curve for Mechanical Measurements

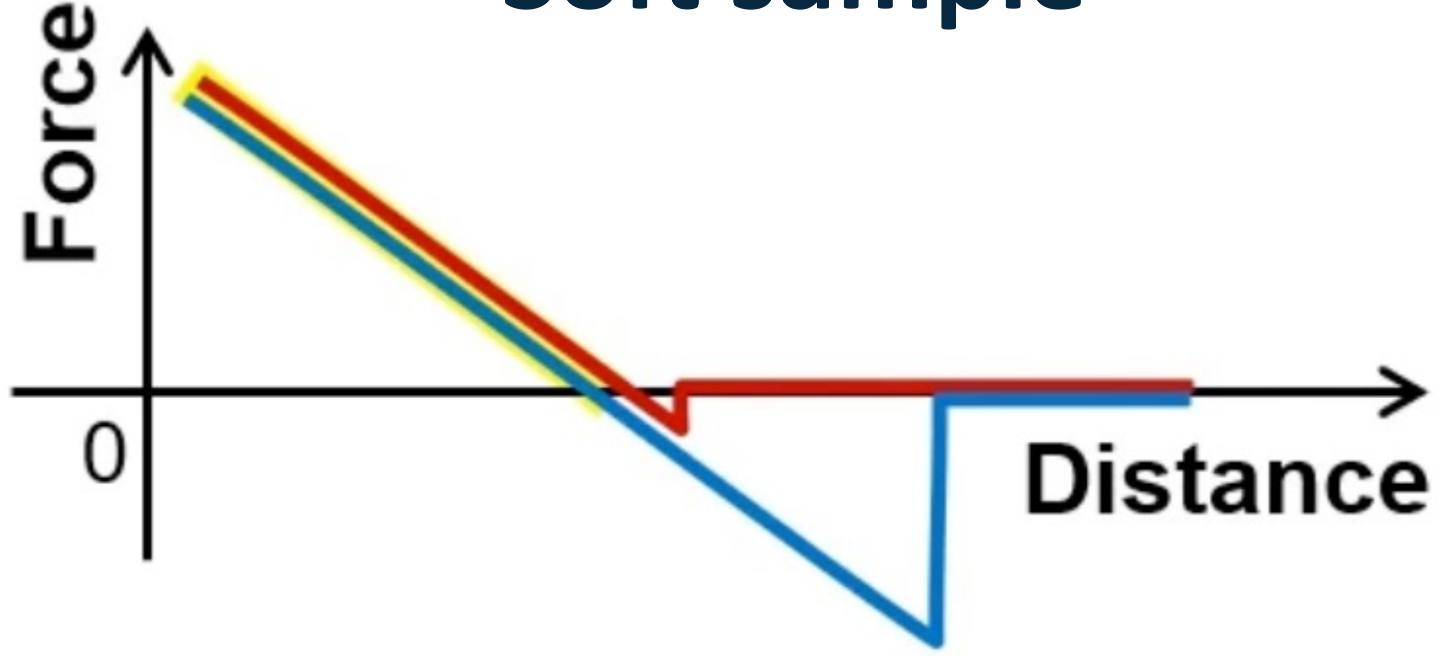


Force-Distance Curve Vary For Different Samples

Hard sample

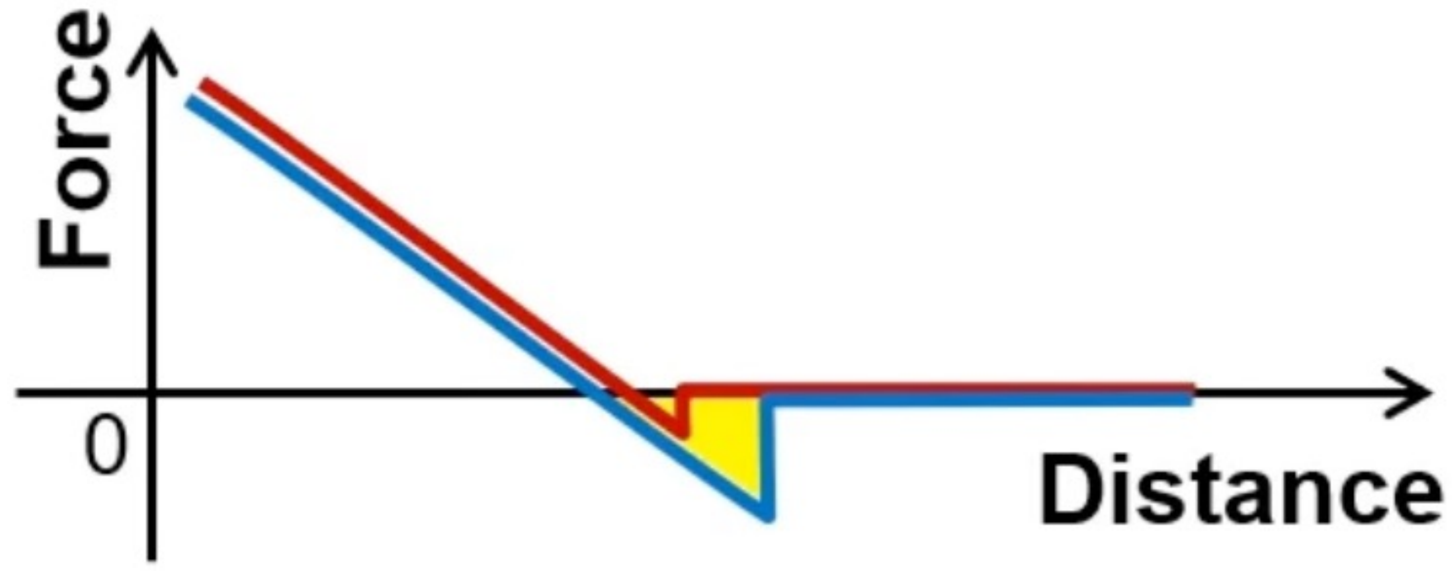


Soft sample

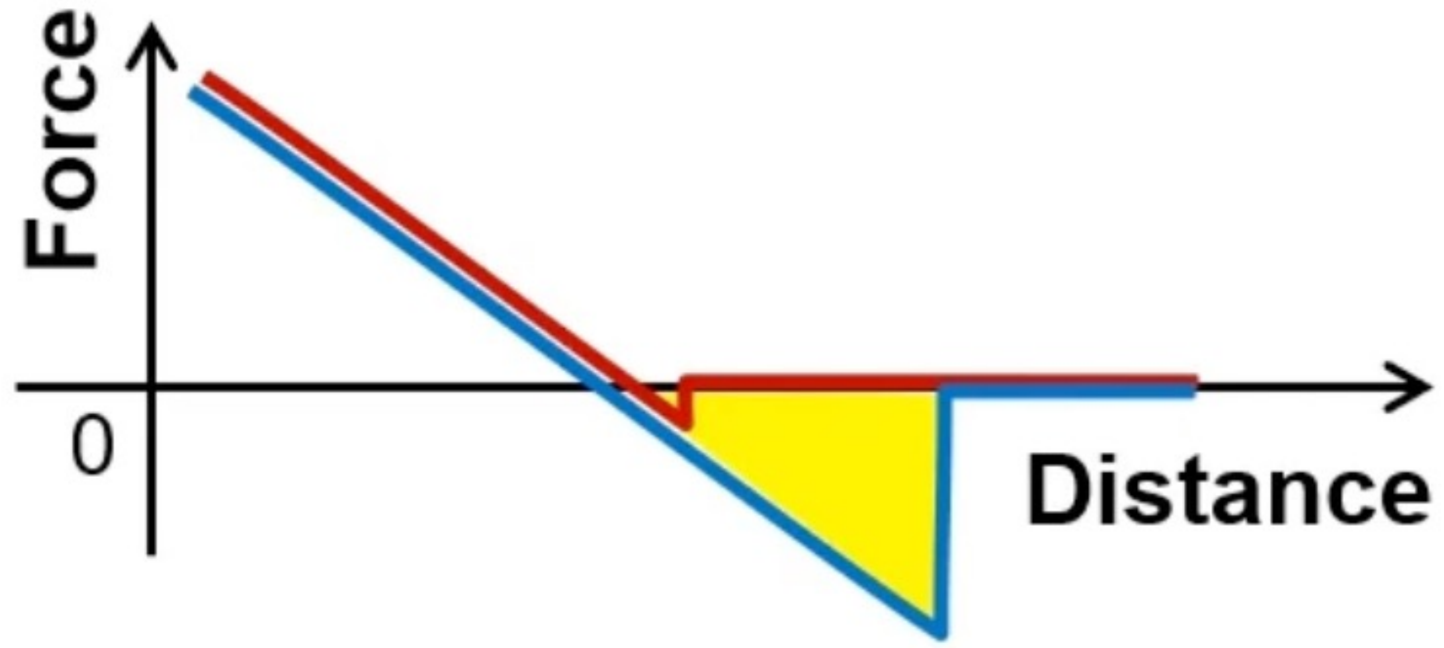


Harder samples have steeper slopes on the force-distance curve

Low adhesive sample

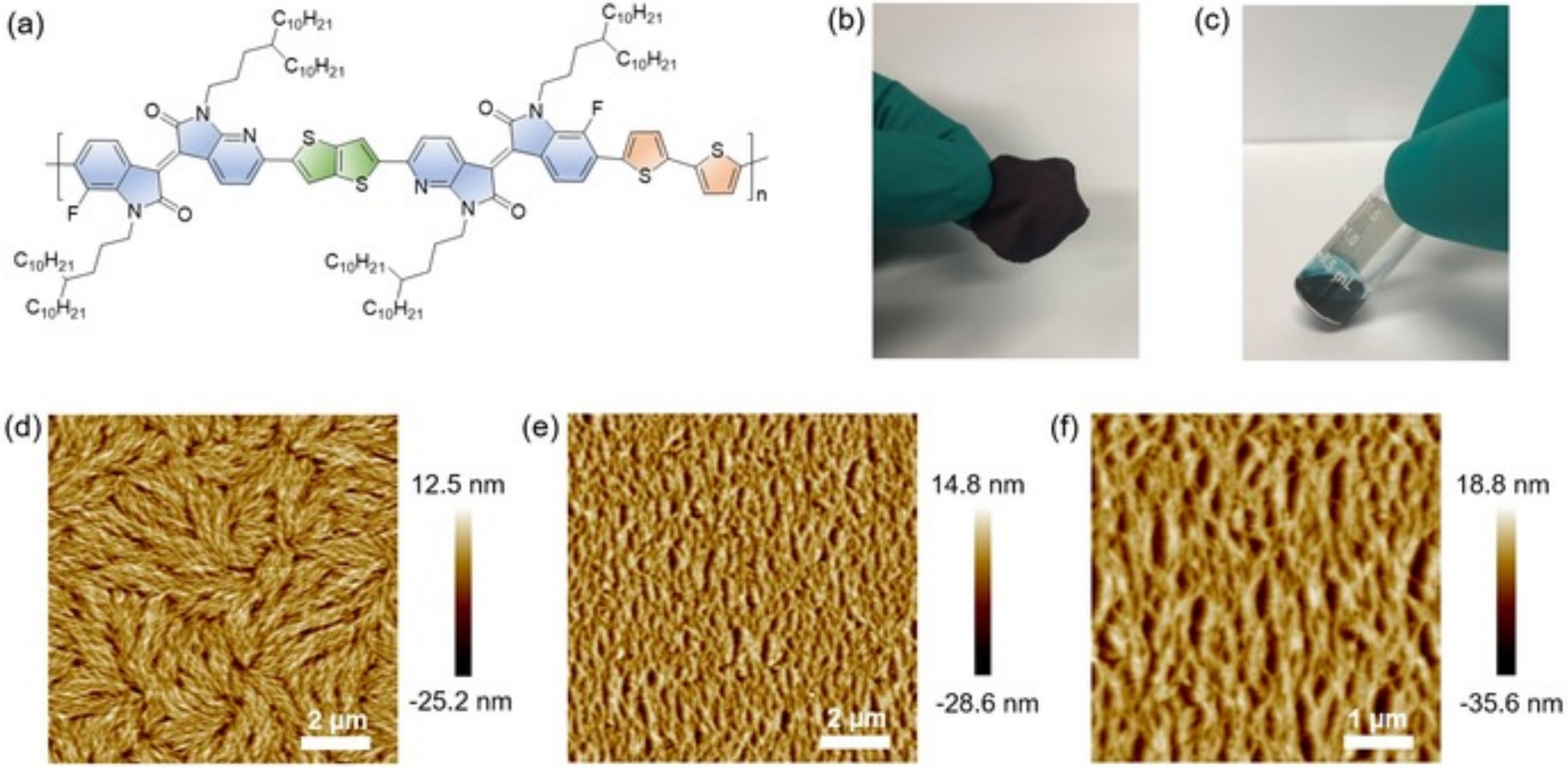


High adhesive sample



Sticky adhesive samples have larger area between retract curve and baseline

AFM Images of Non-Conductive Polymer Films



Yang, *et al.* | *Nat. Sci. Rev.* | **2021**

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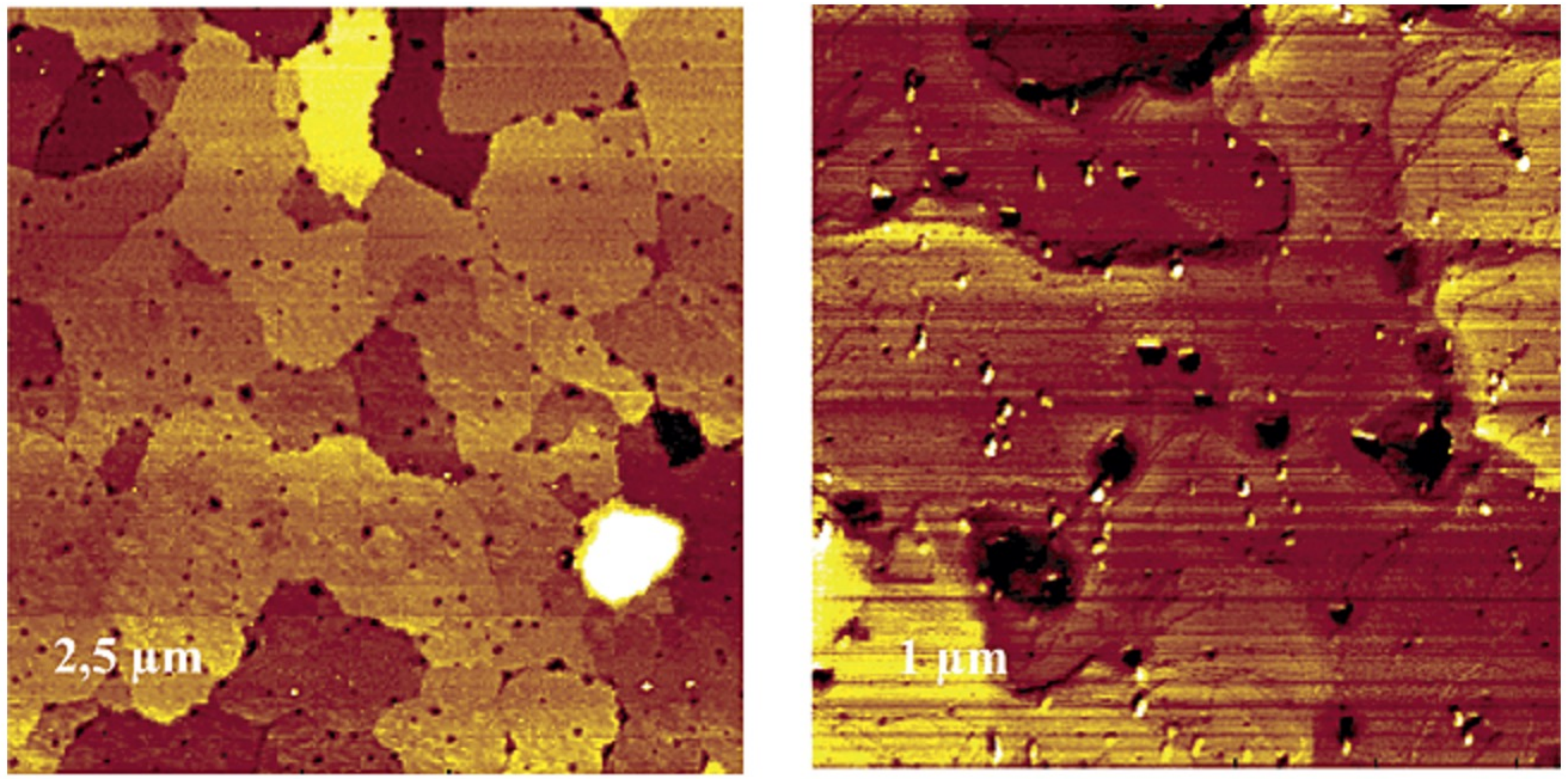
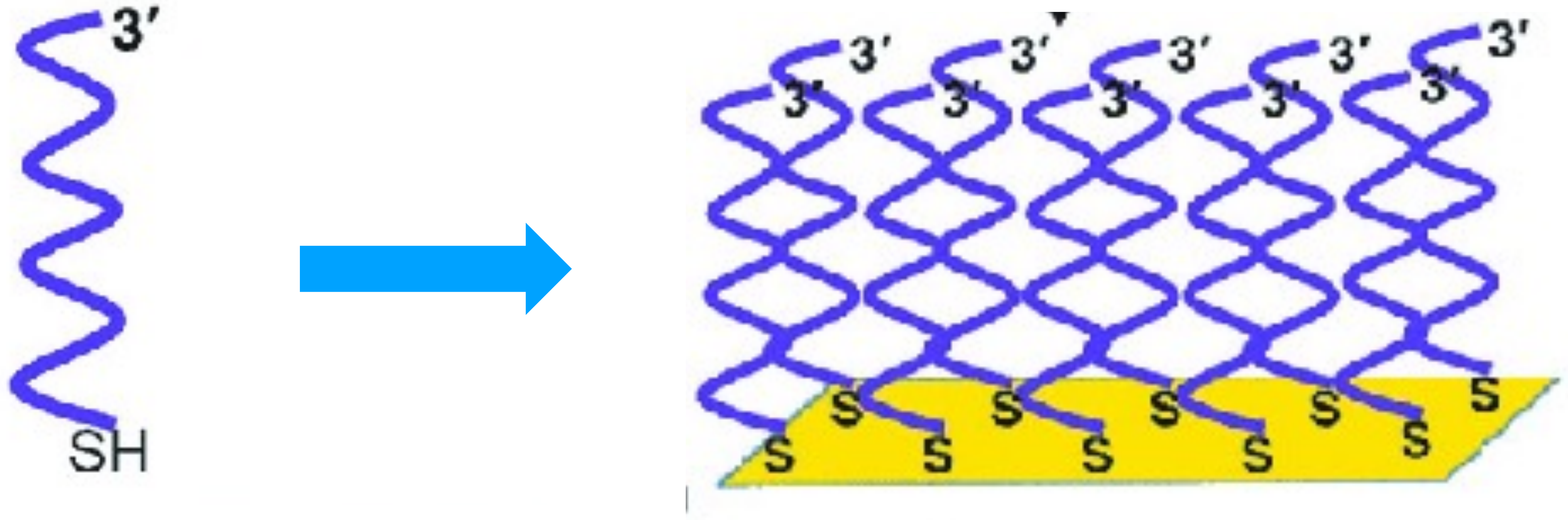
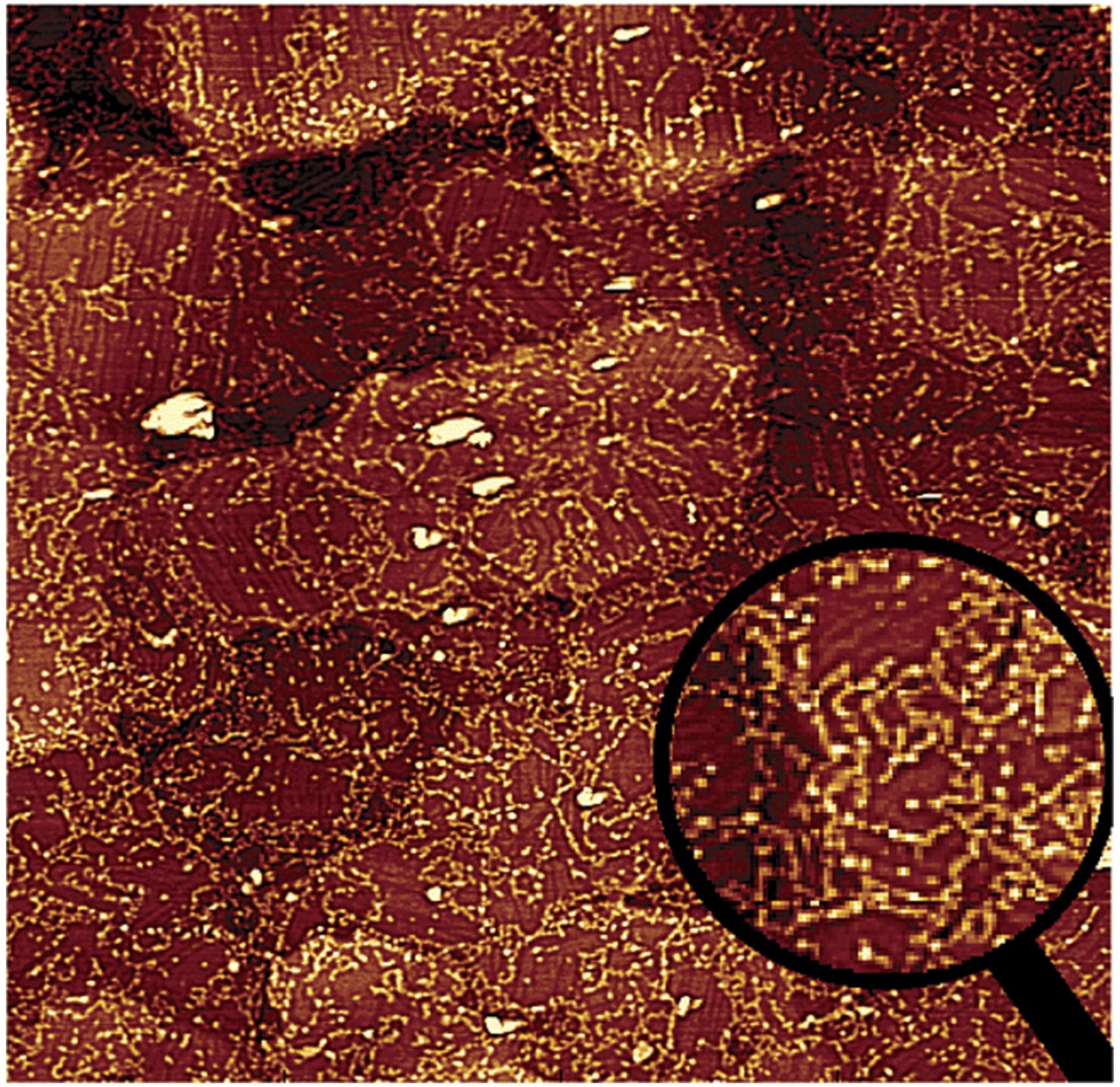
AFM to Visualize Molecular Assembly on Surfaces (Thiolated DNA)



AFM image of Au (111) surface (terraces observed)



Surface exposed to a solution of oligonucleotides (25-base thiolated DNA)



2 µm

Mourougou-Candoni, *et al.* | *Langmuir* | **2003**

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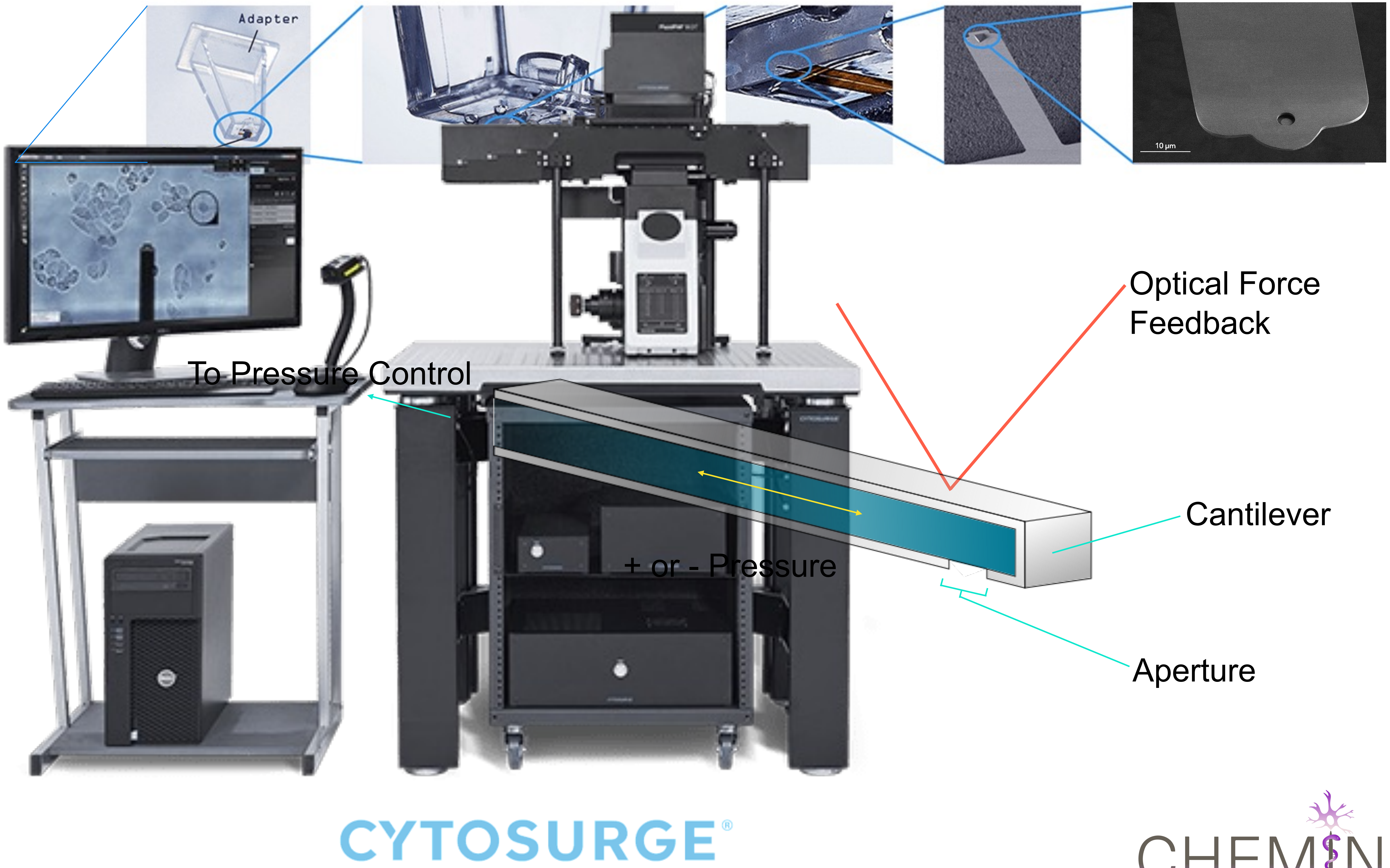
Advances in AFM – the Fluid Force Microscope (FluidFM)



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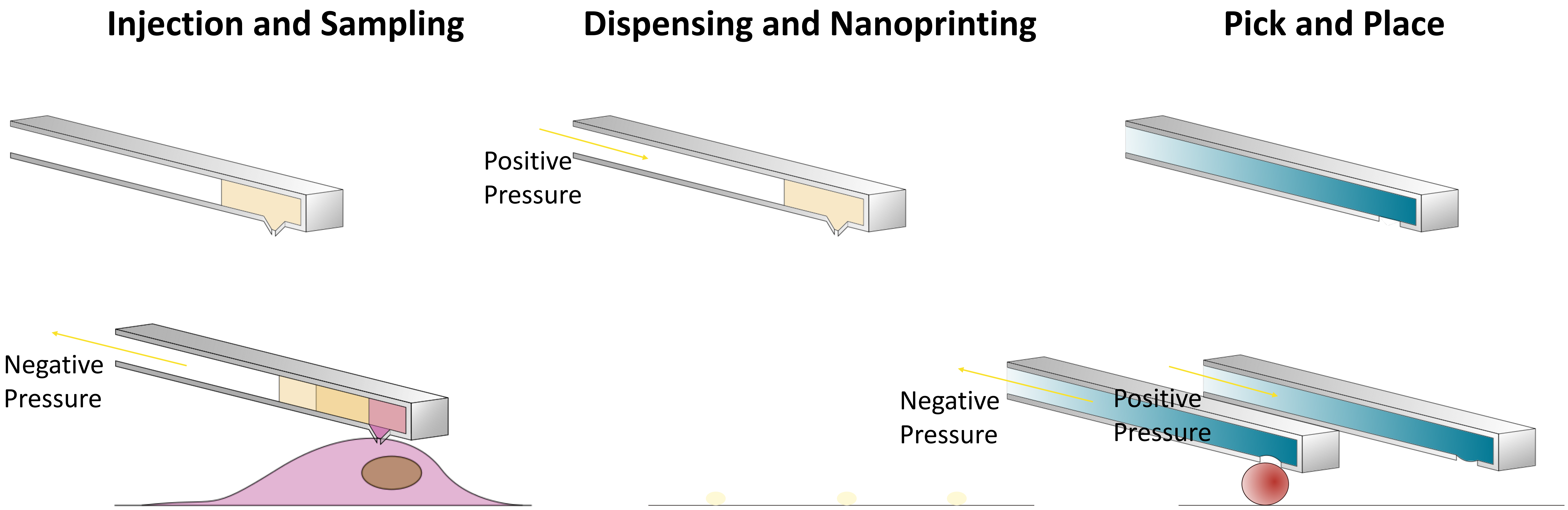
Advances in AFM – the Fluid Force Microscope (FluidFM)



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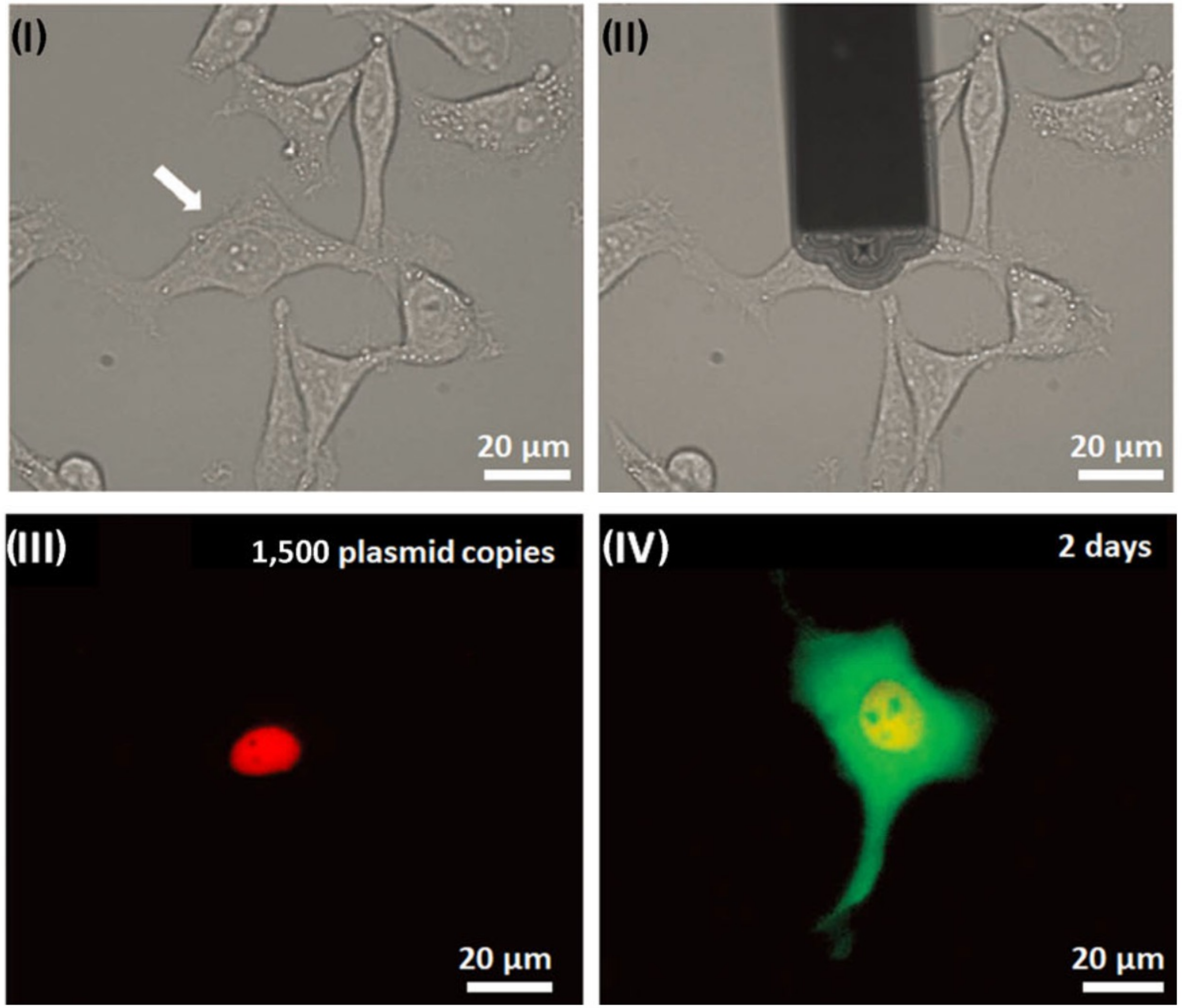
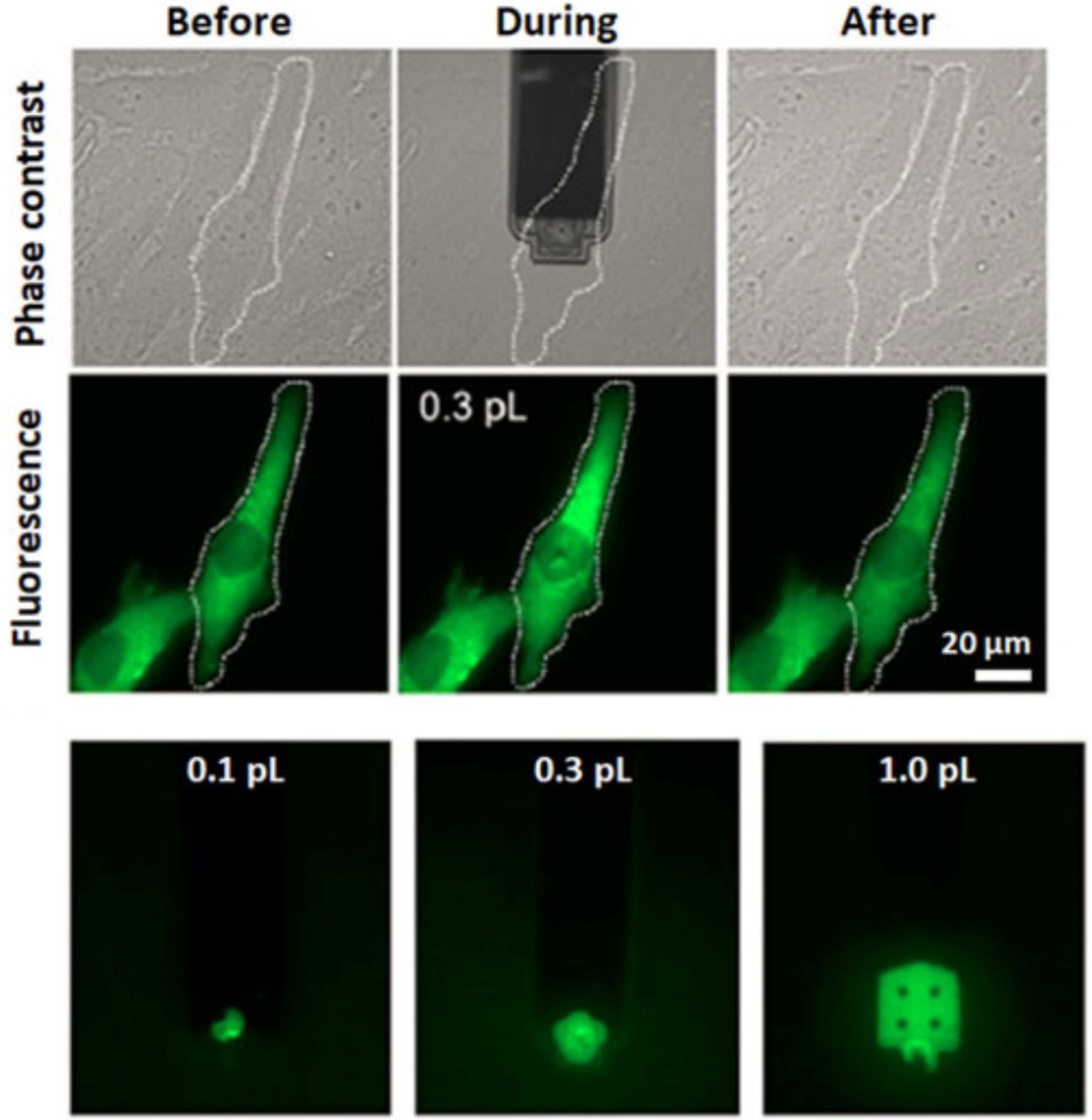
Applications of Using FluidFM and Interfacing with Cells

Delivering plasmid DNA to cell nucleus



Extract from nucleus (82% viability for 4.0 pL)



Li, *et al.* | *Nano Res.* | **2022**

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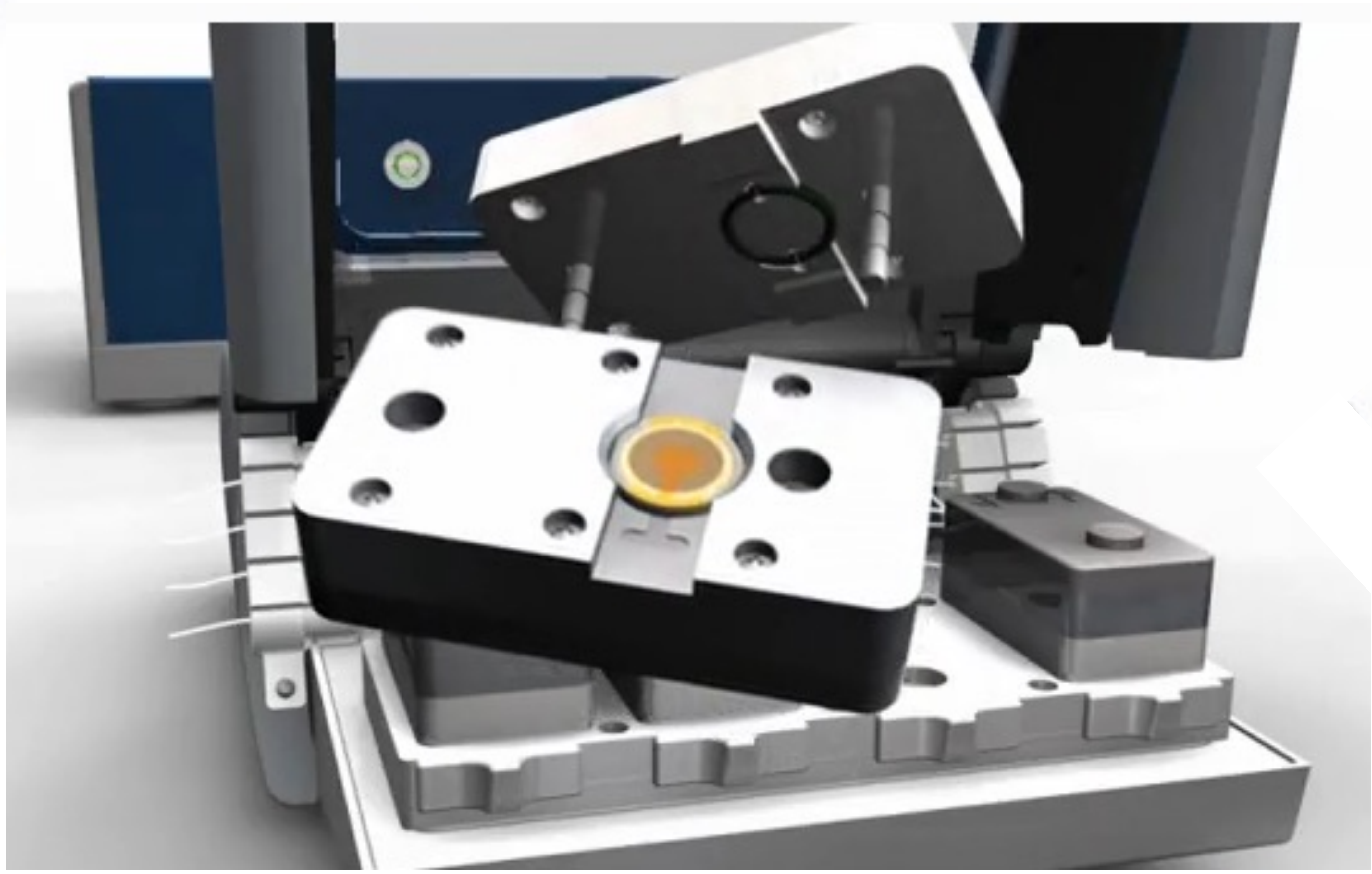
Key Takeaways

- Comparisons between AFM and STM – pros and cons
- How AFM can go from surface imaging to mechanical properties
- Contact *vs.* non-contact mode AFM
- How to measure forces at surfaces using AFM
- Fluid-force microscopy (FluidFM) to interact with biology

Quartz-Crystal Microbalance (QCM) – Monitoring Surface Dynamics



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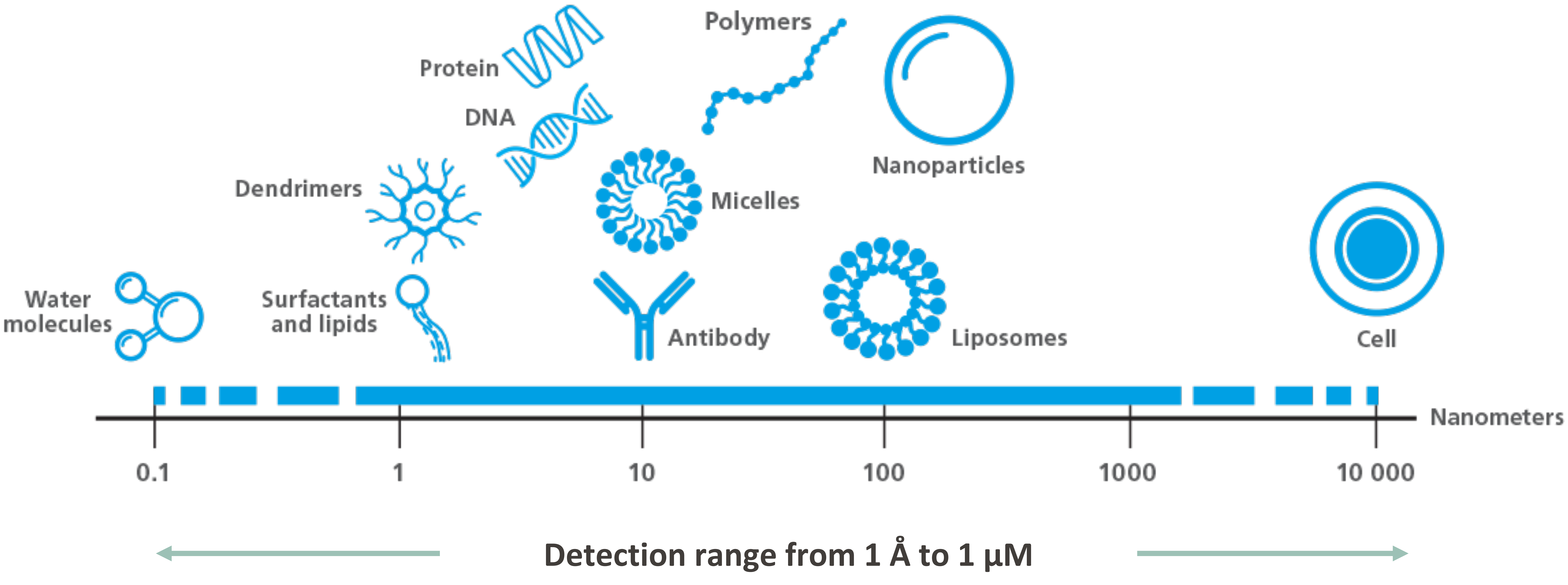
Quartz-Crystal Microbalance (QCM) – Monitoring Surface Dynamics

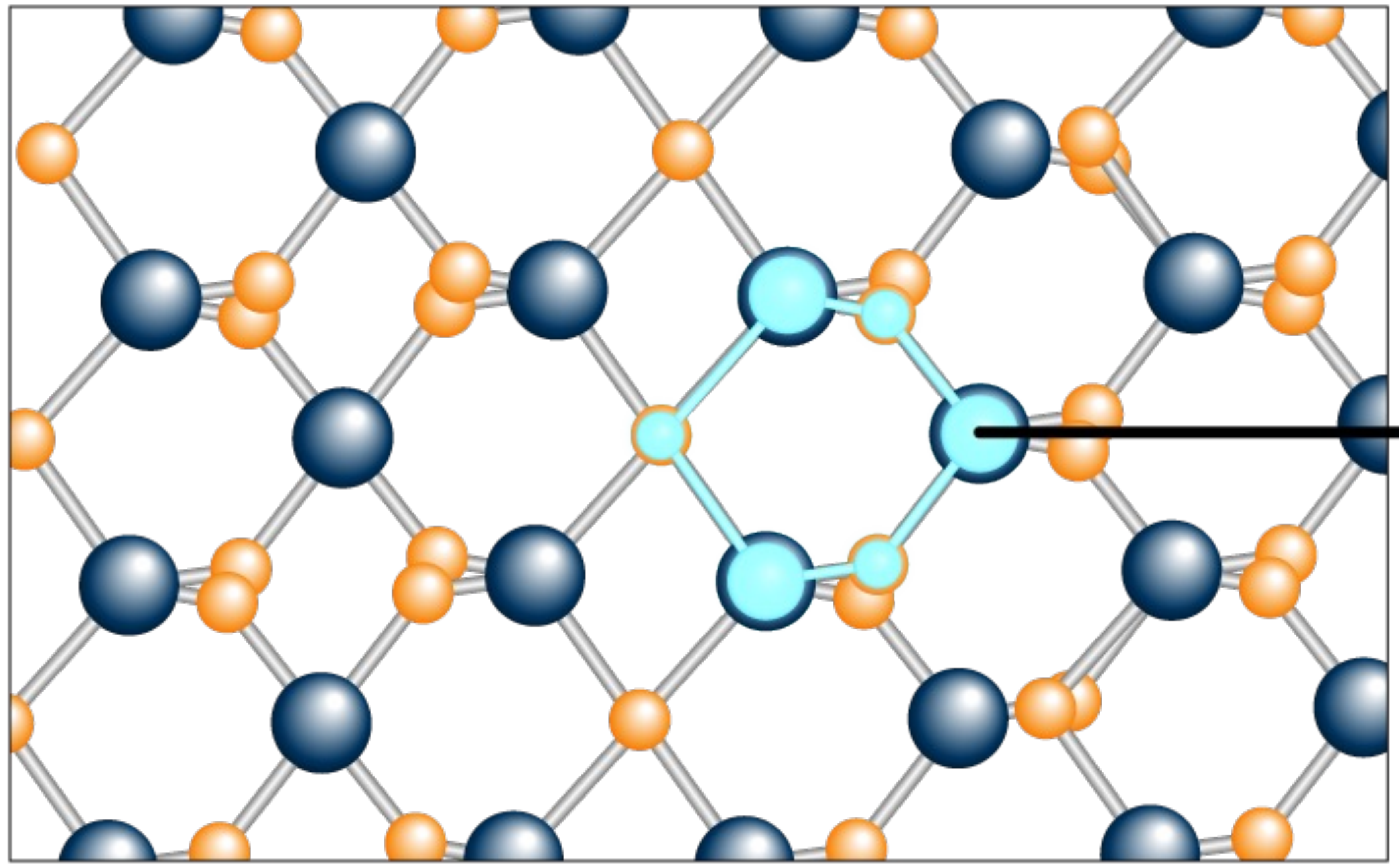


Quartz as a Piezoelectric Material

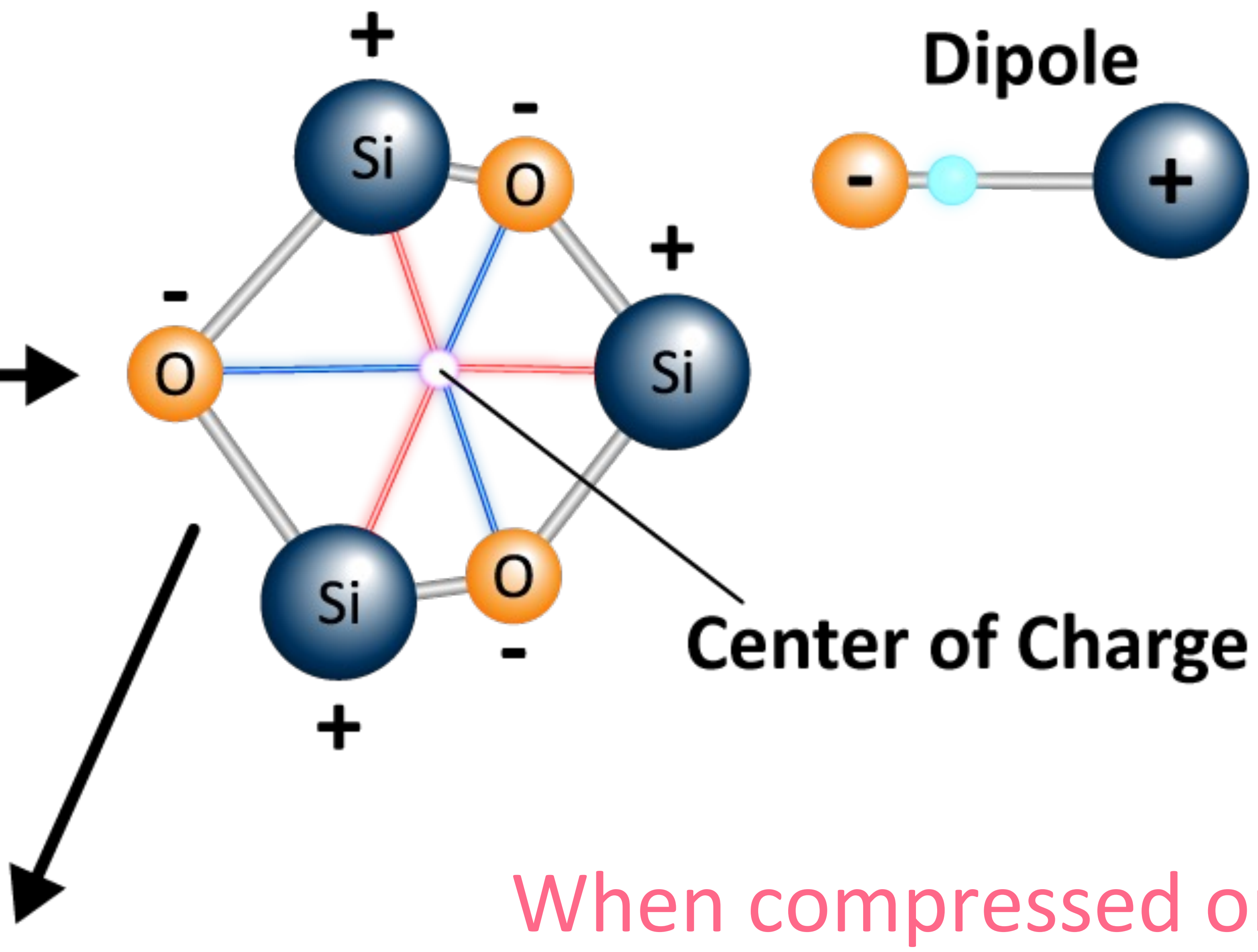
Abundant in nature

Easy to grow and process

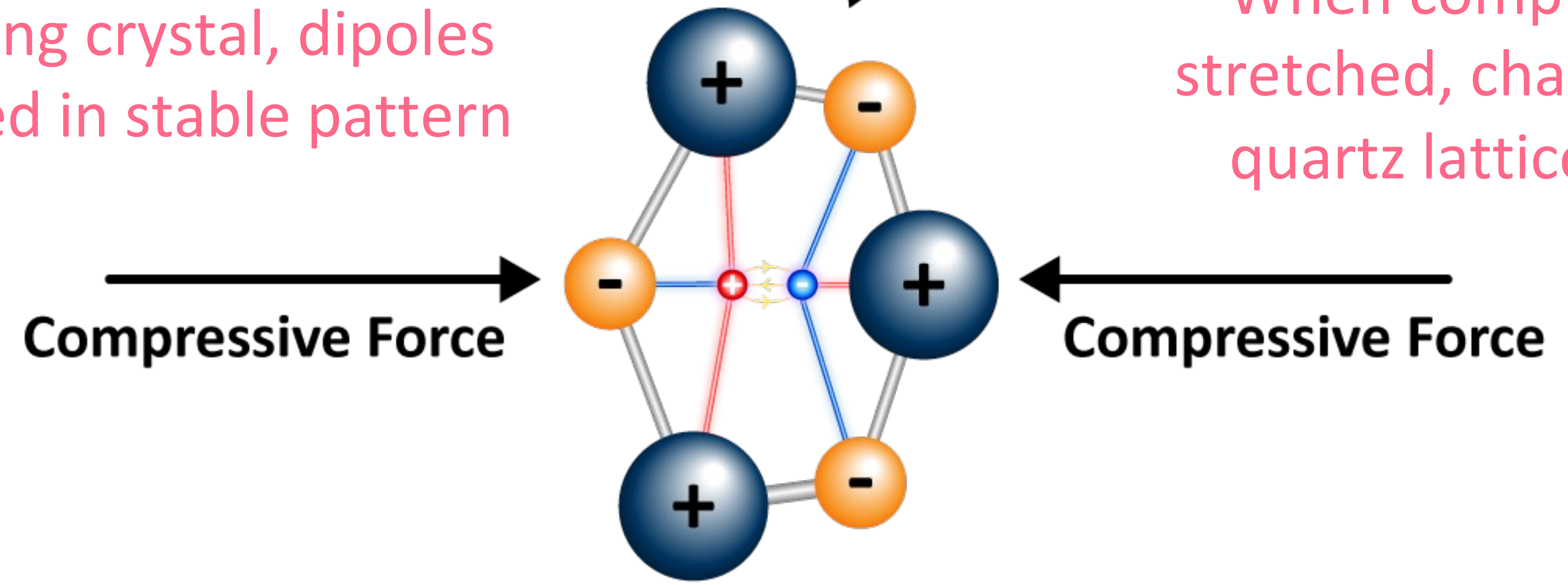
Thermodynamically stable



In resting crystal, dipoles arranged in stable pattern



When compressed or stretched, charges within quartz lattice shift ➔

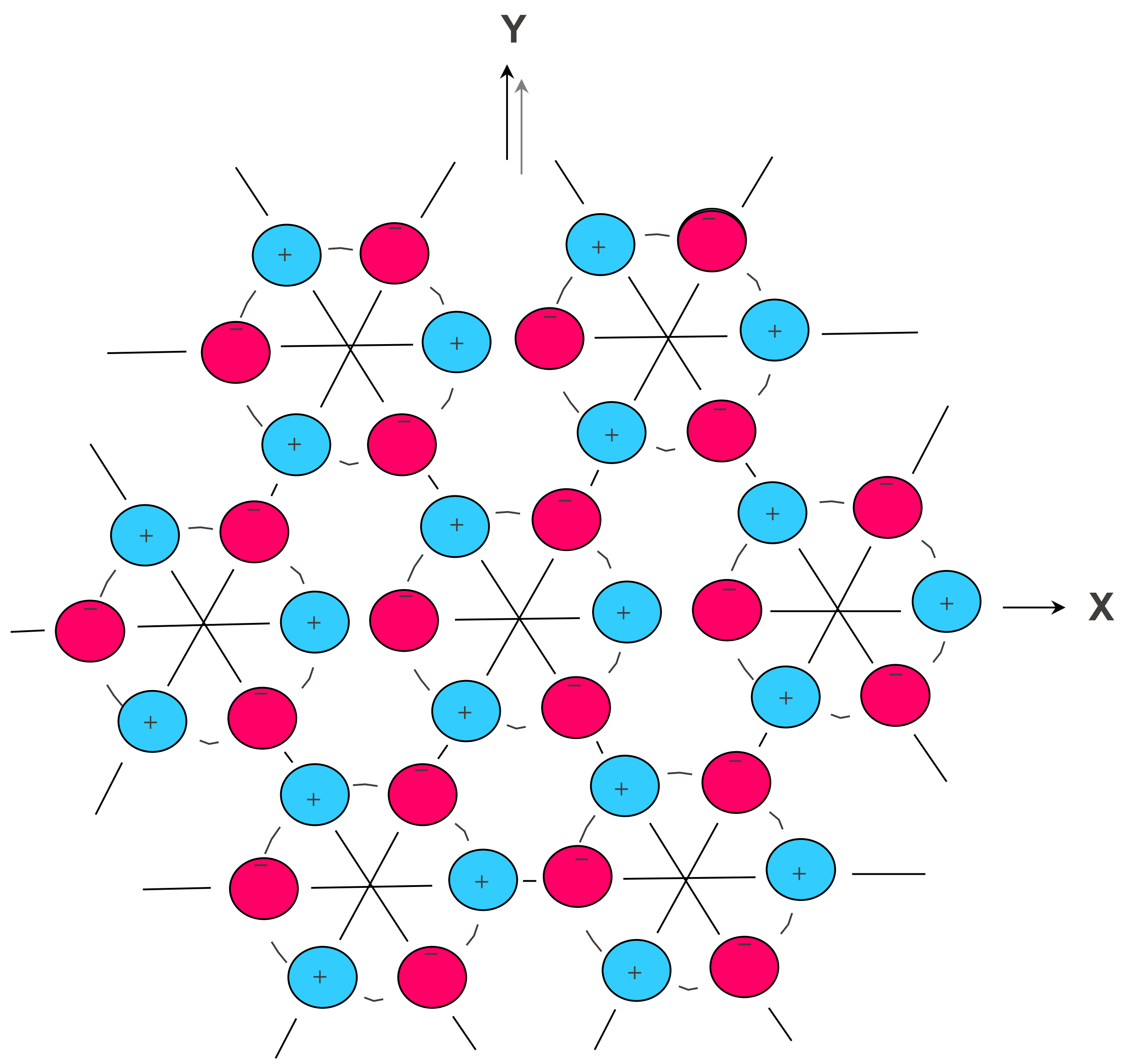


Resonant Frequency of Quartz and Oscillation Amplitude

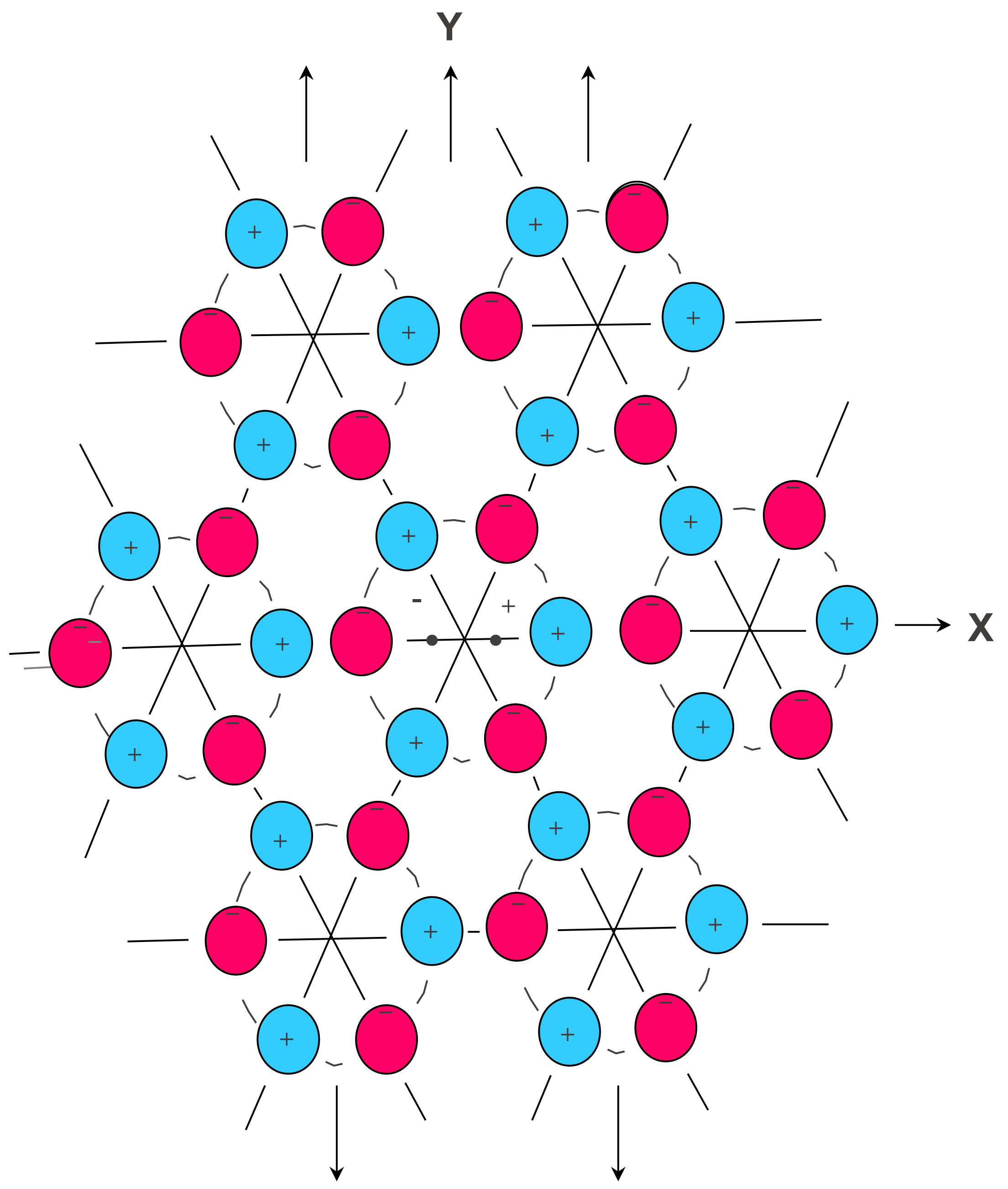
Resonant frequency: frequency at which quartz crystal vibrates most efficiently when energy is applied.

At this frequency, layers of atoms within the crystal lattice slide smoothly and consistently in shear motion.

Quartz oscillates with maximum efficiency → Achieve greatest amplitude while minimizing energy loss



Undeformed lattice



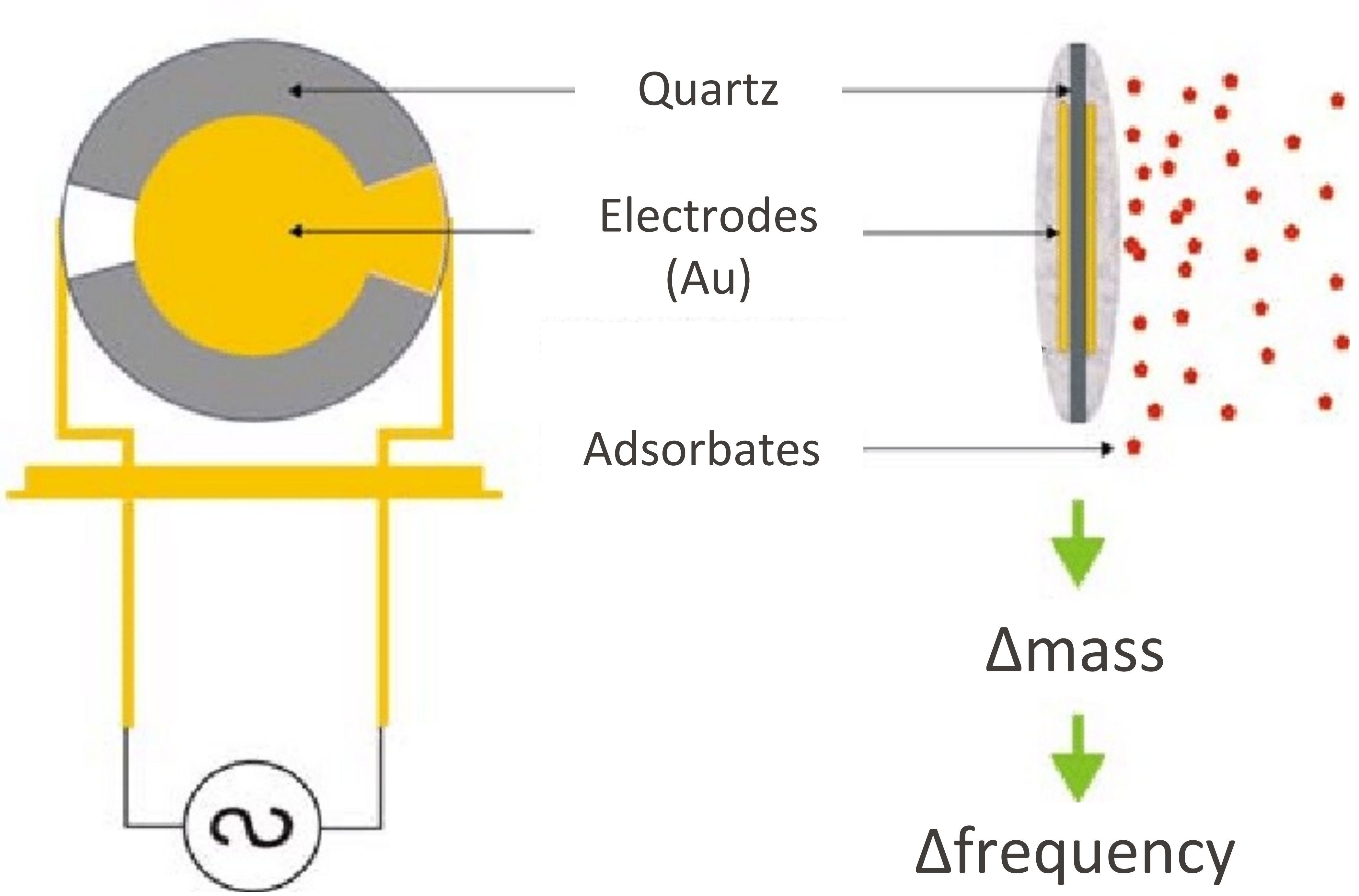
Strained lattice

Credit: Janos Voros

From Quartz to QCM-D

Piezoelectricity
Piezin, Greek *”to press”* → Resonator → Balance

Quartz crystal disk sandwiched between two electrodes → Quartz piezoelectric – applied electric field (voltage) leads to mechanical deformation



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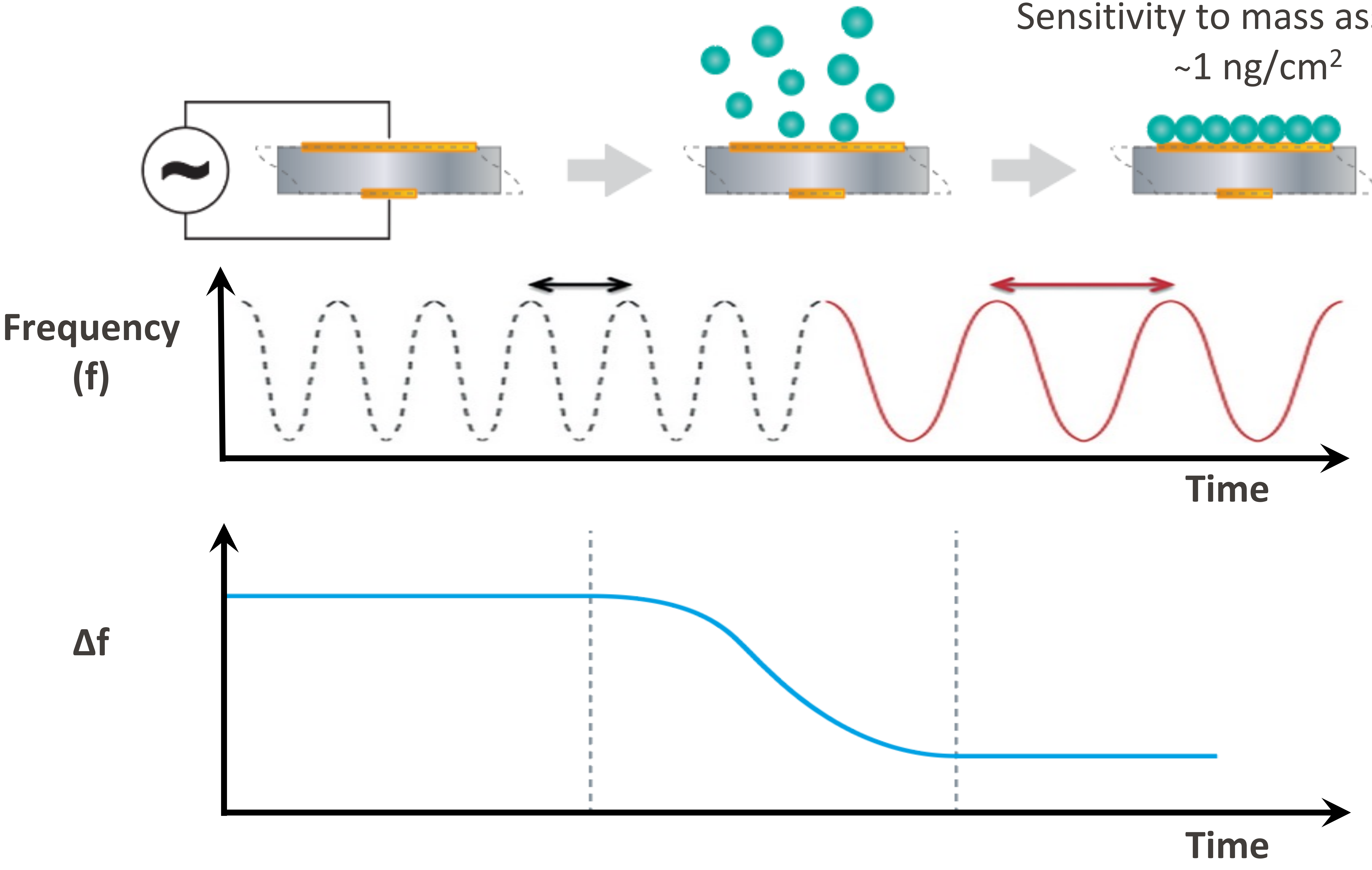
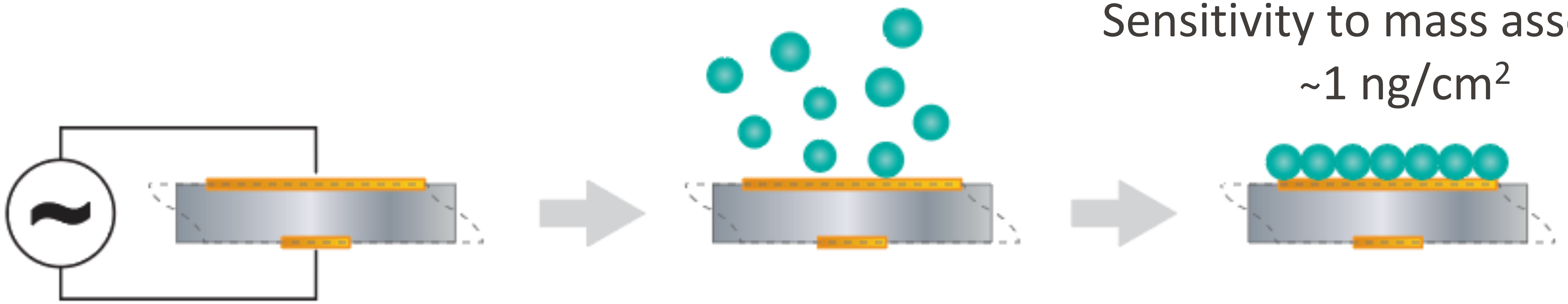
Mass Assembly Monitored Through Change in Frequency

Sensitivity to mass assembly:
~1 ng/cm^2



Sauerbrey Equation

Sensitivity to mass assembly:
~1 ng/cm^2



Ability of the QCM to measure mass changes based on discovery of the relation between the resonance frequency and mass by Günter Sauerbrey (1959)

$$\Delta m = -C \cdot \frac{\Delta f}{n}$$

Δm: mass change
Δf: change in resonance frequency
C is the mass sensitivity constant = 17.7 ng/(cm^2 · Hz) for 5 MHz quartz crystal
n: harmonic number (1, 3, 5, ...)

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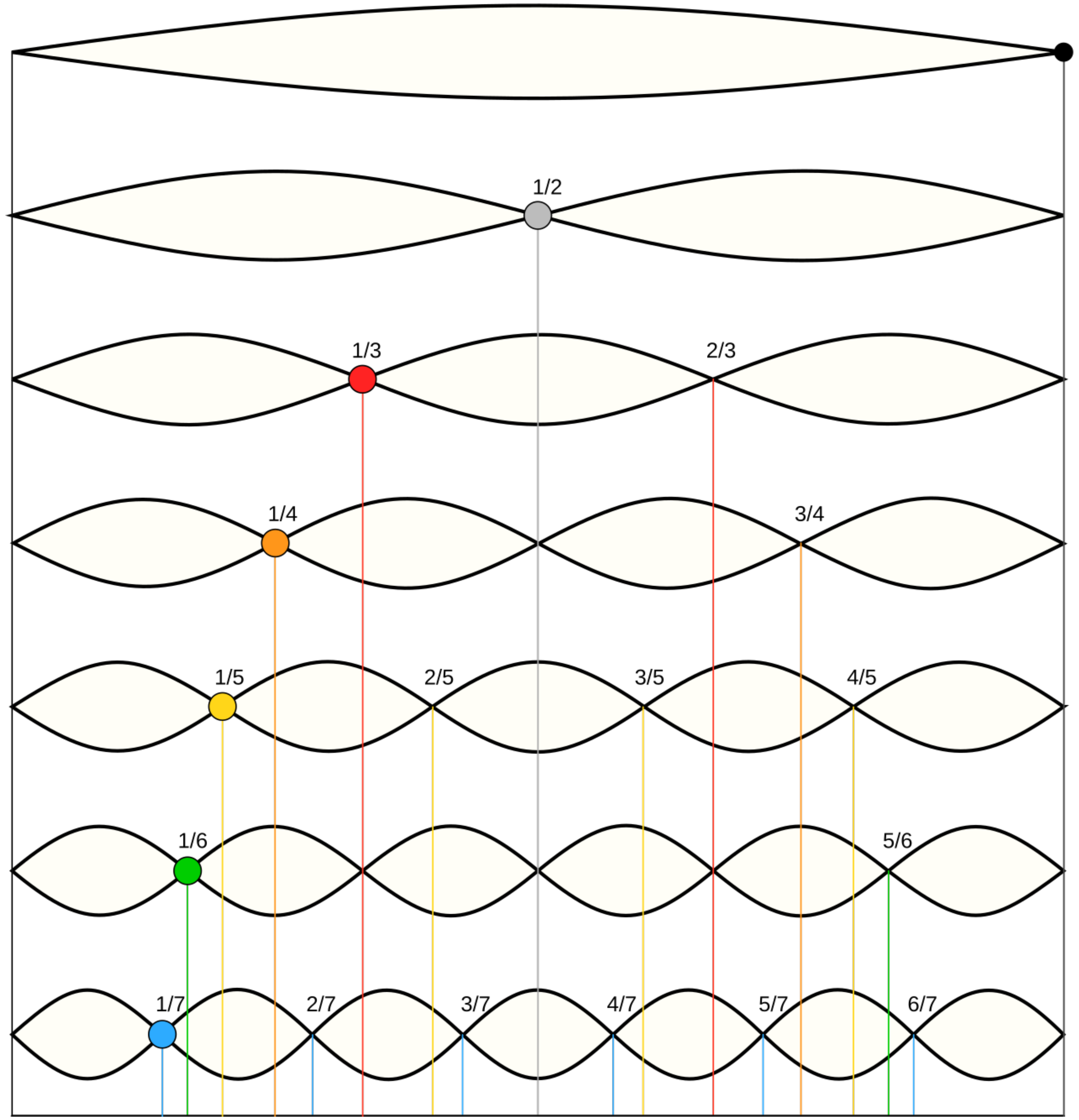
Harmonics in QCM-D



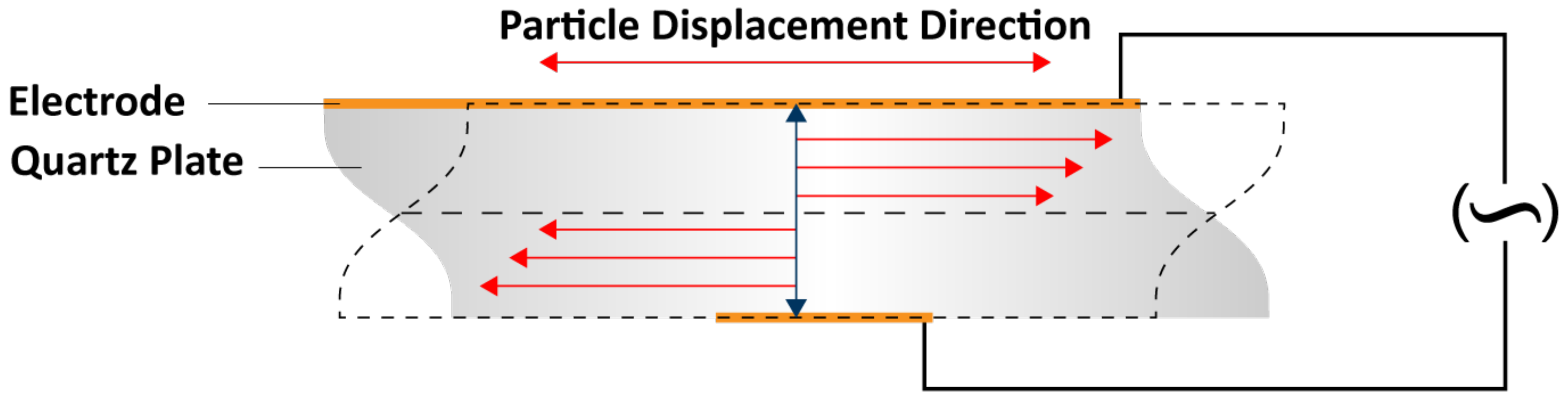
Source: Wikipedia

In physics, harmonics are the different standing-wave patterns a system can vibrate in, each with its own frequency

Fundamental mode – slowest vibration

Higher harmonics – faster vibrations

In QCM-D, we only use odd harmonics (1, 3, 5, 7…) because only those patterns make the top and bottom surfaces move in the same phase



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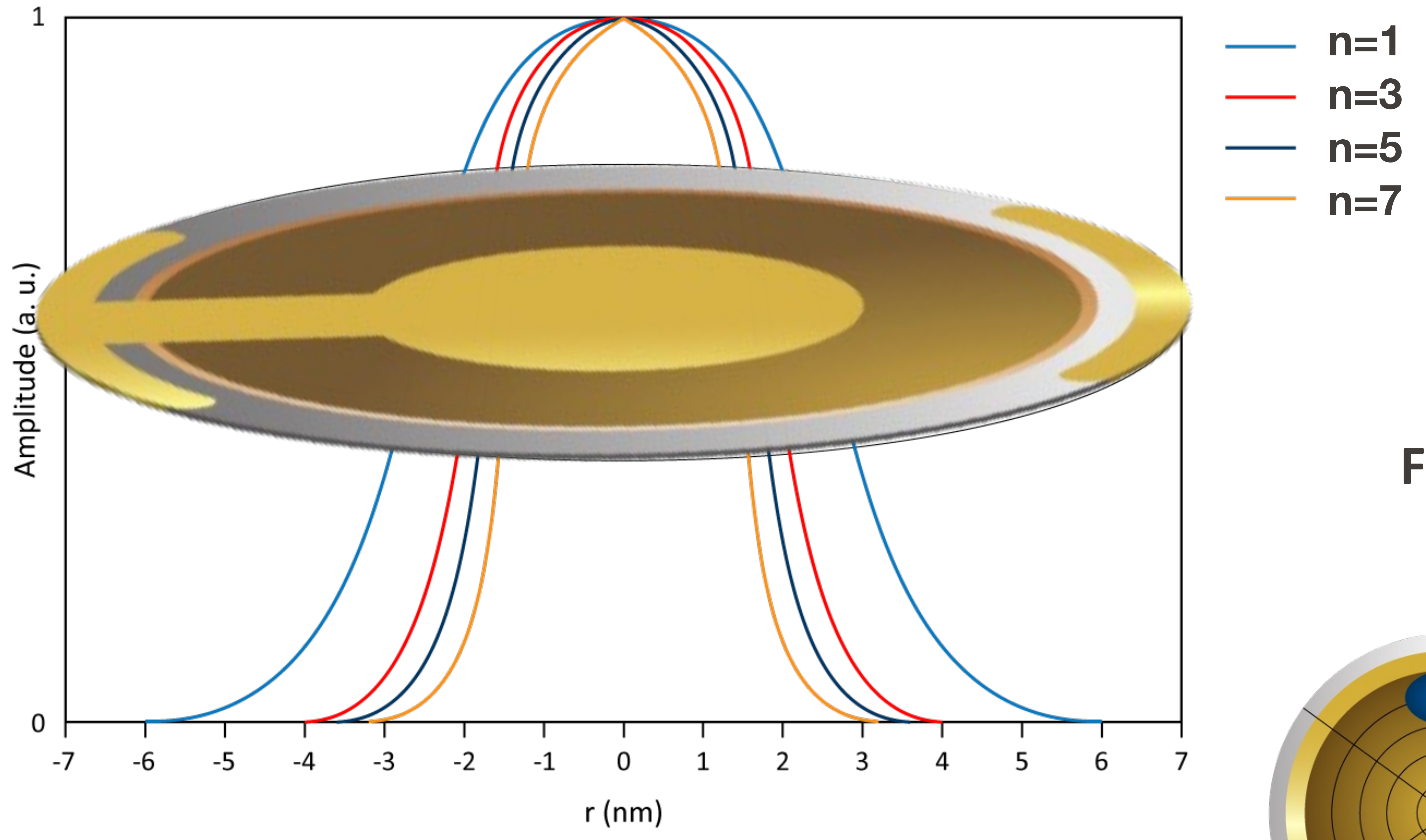
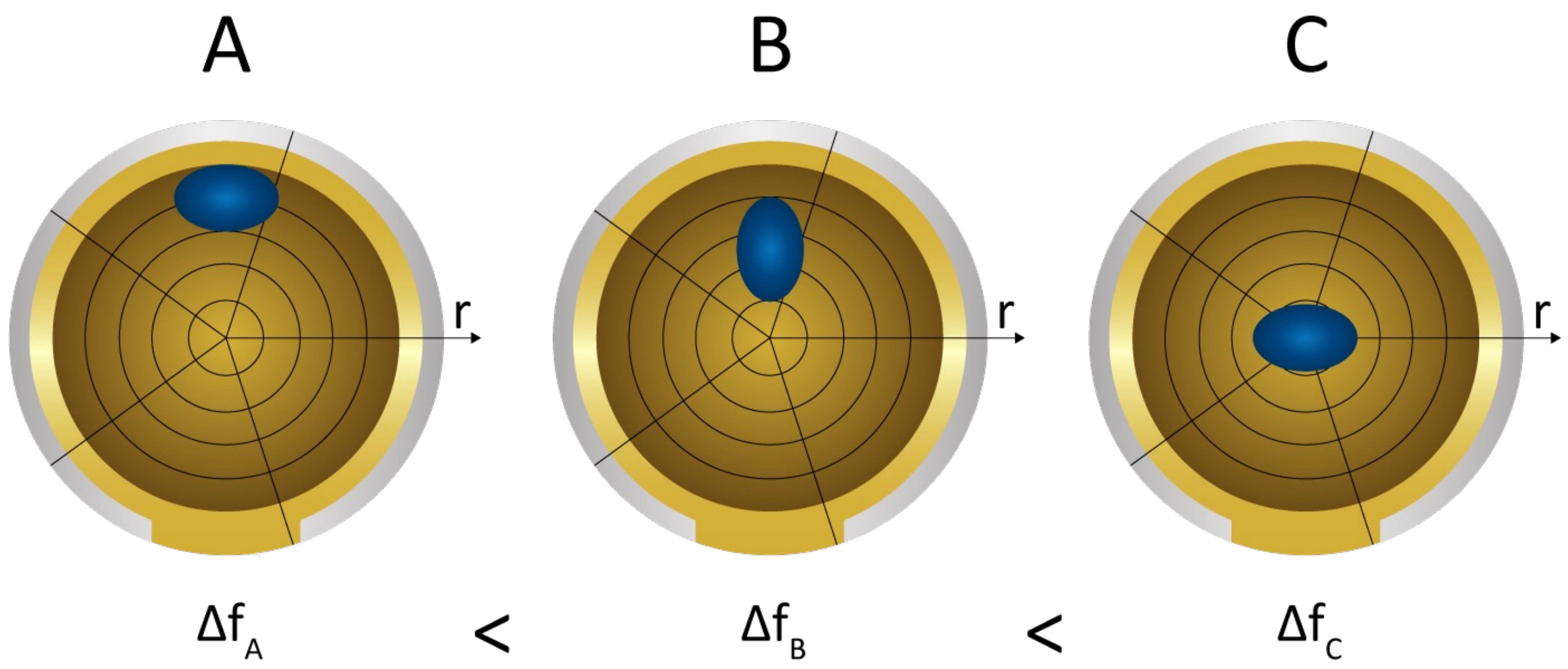
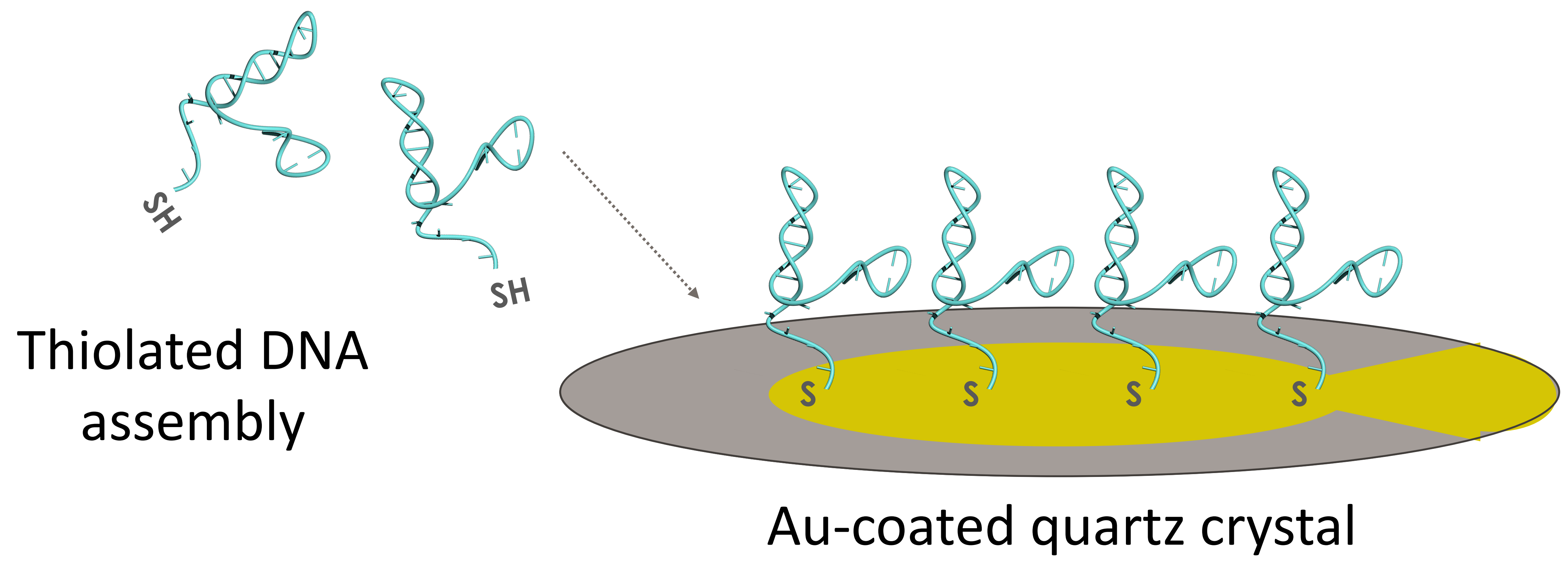
Sensitivity Near the Center of the Sensor



Frequency shift based on sample location



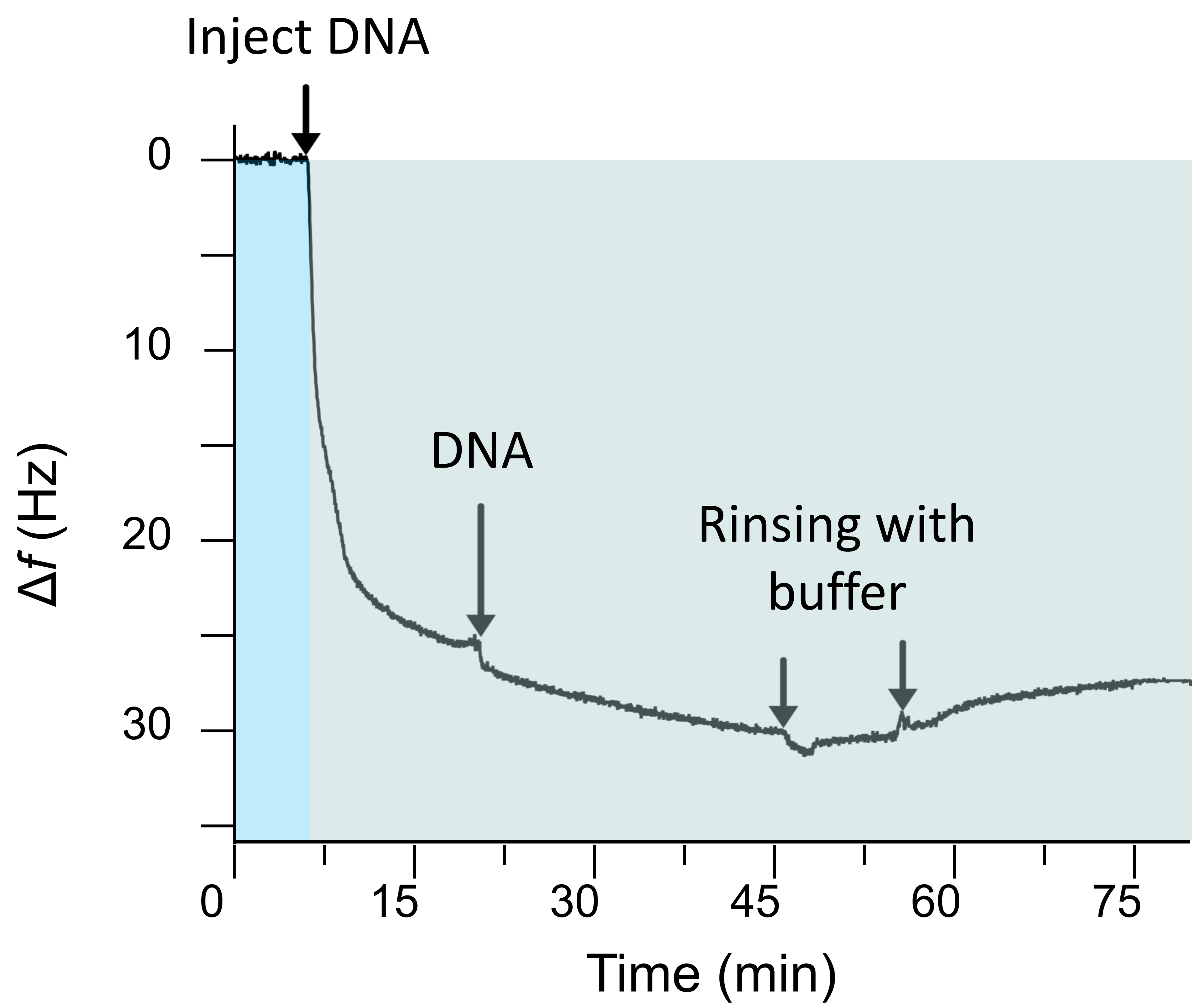
Quartz-Crystal Microbalance to Monitor DNA Assembly on Surface

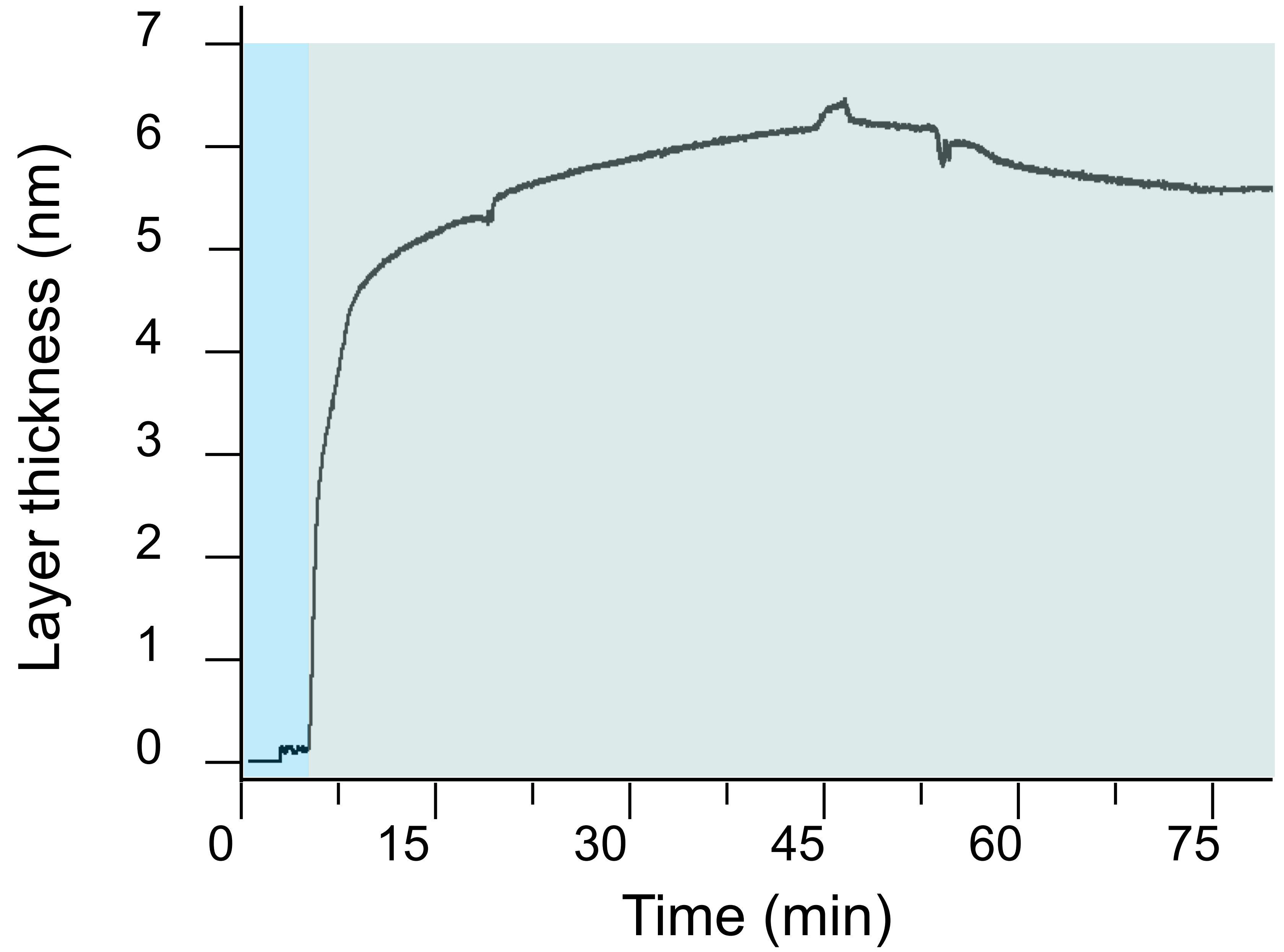


Sauerbrey equation

$$\Delta m = -\frac{\Delta f}{C}$$

$$d = \frac{\Delta m}{\rho}$$



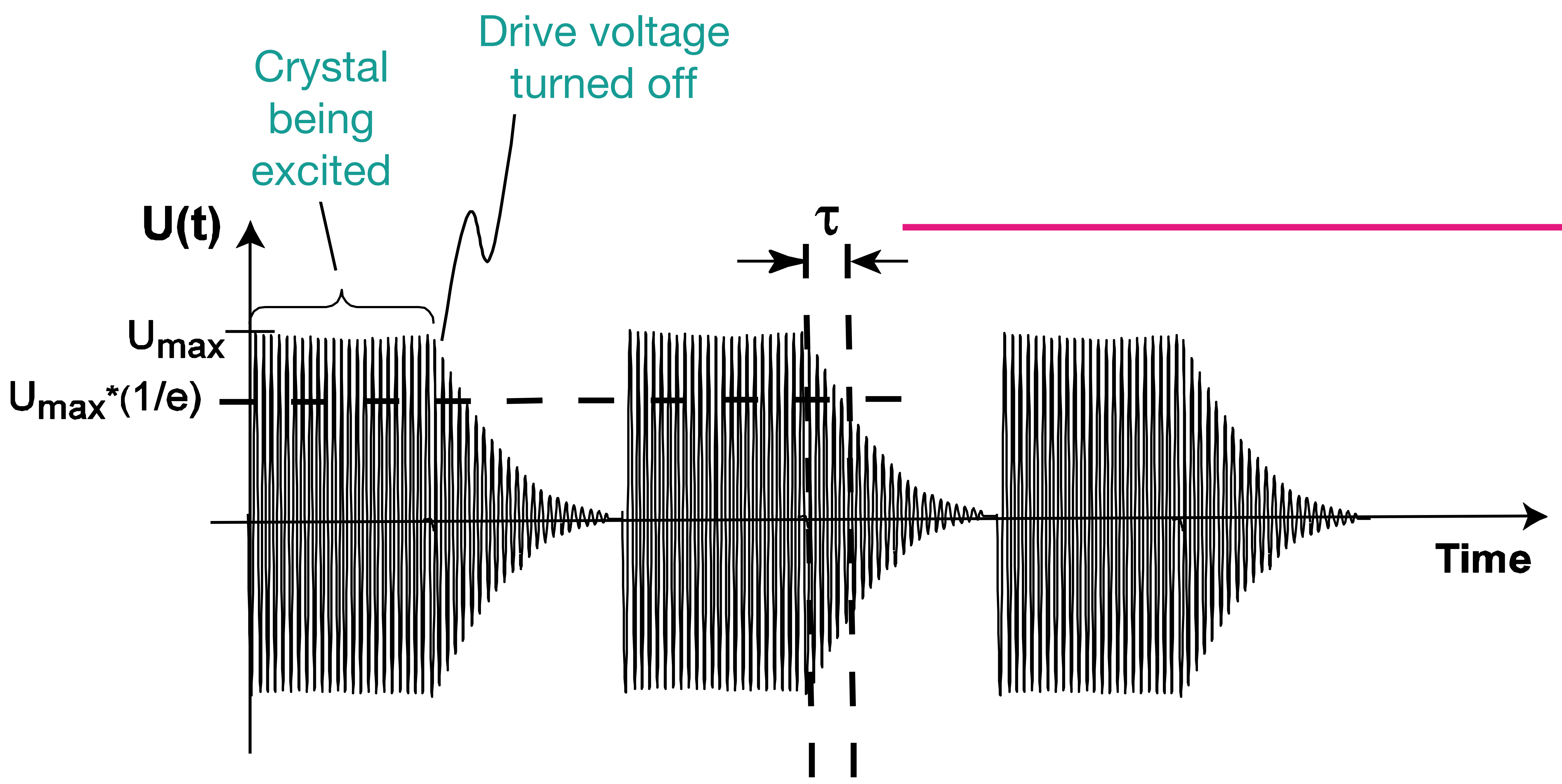


Nakatsuka *et al.* | *Anal. Chem.* | 2021

Quartz-Crystal Microbalance With Dissipation Monitoring

We can also extract information on the viscoelastic properties of soft, viscous layers

Dissipation data reveals characteristics of non-rigid layers that undergo internal rearrangements and energy loss



Dissipation

$$D = \frac{1}{\pi f \tau}$$

Rodahl *et al.*, | *Rev Sci Instr.* | 1995

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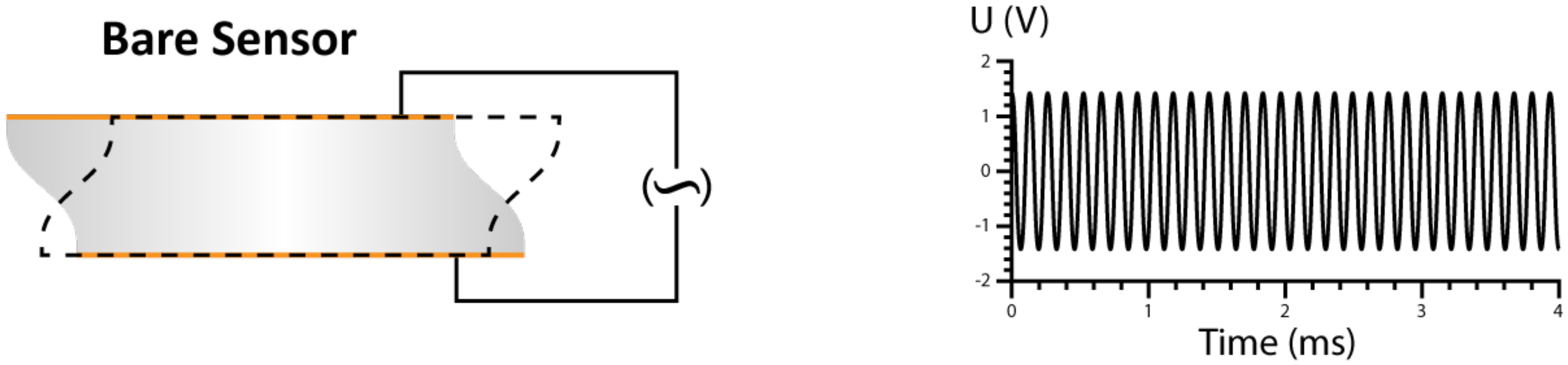
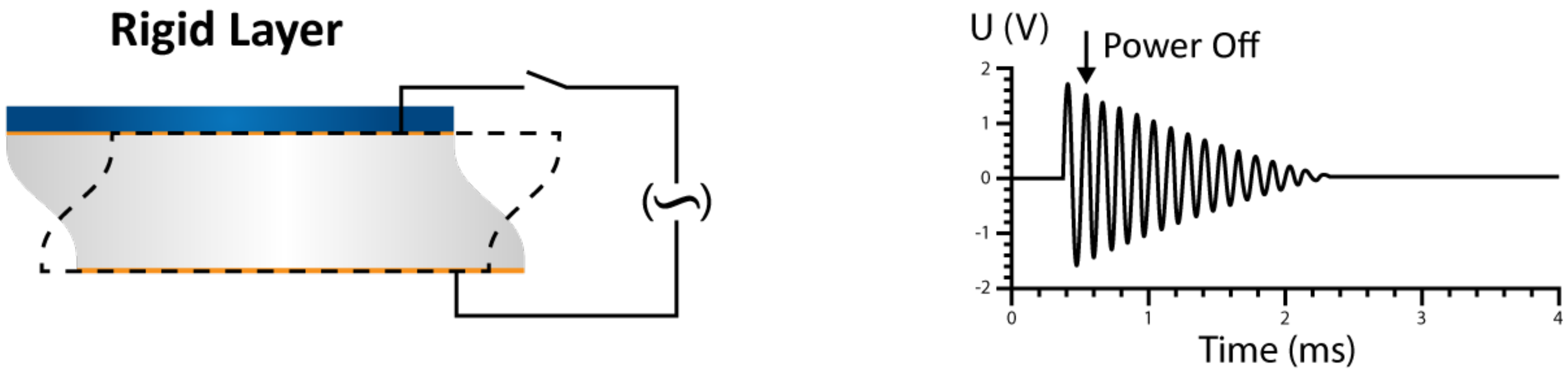
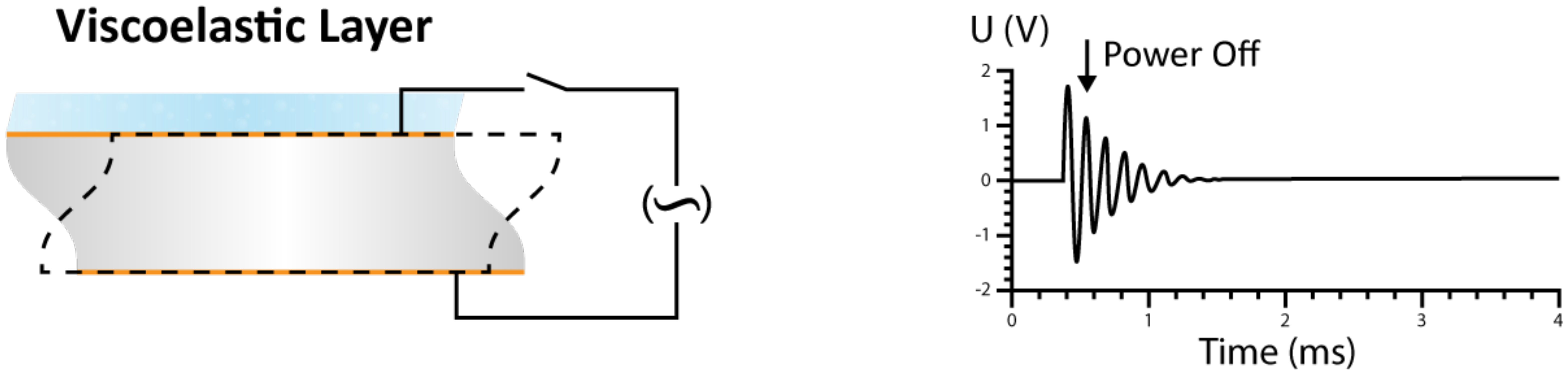
Quartz-Crystal Microbalance With Dissipation Monitoring



Rigid materials show slower decay due to stronger coupling with quartz



Exponential decay of oscillation amplitude once voltage turned off



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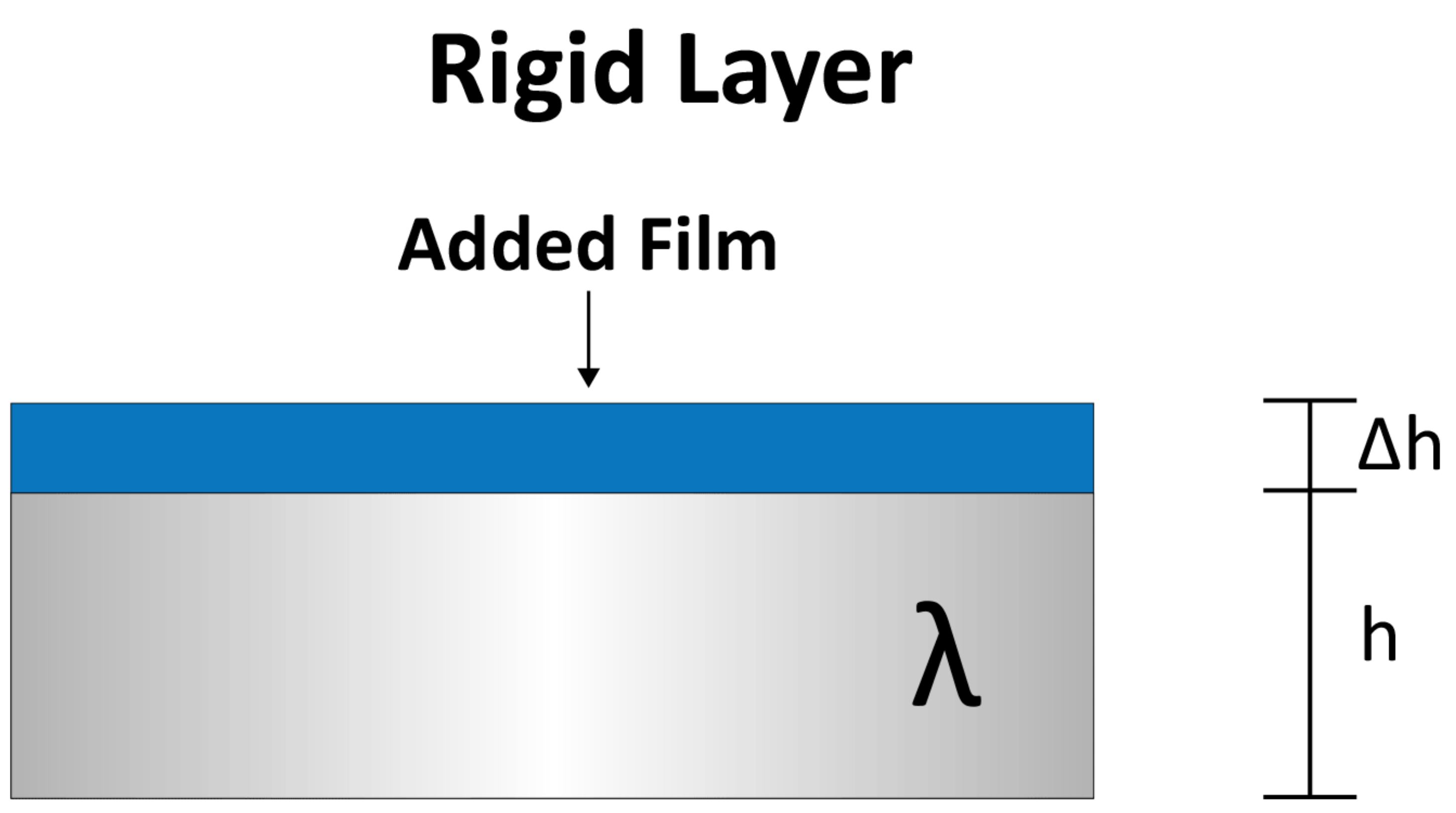
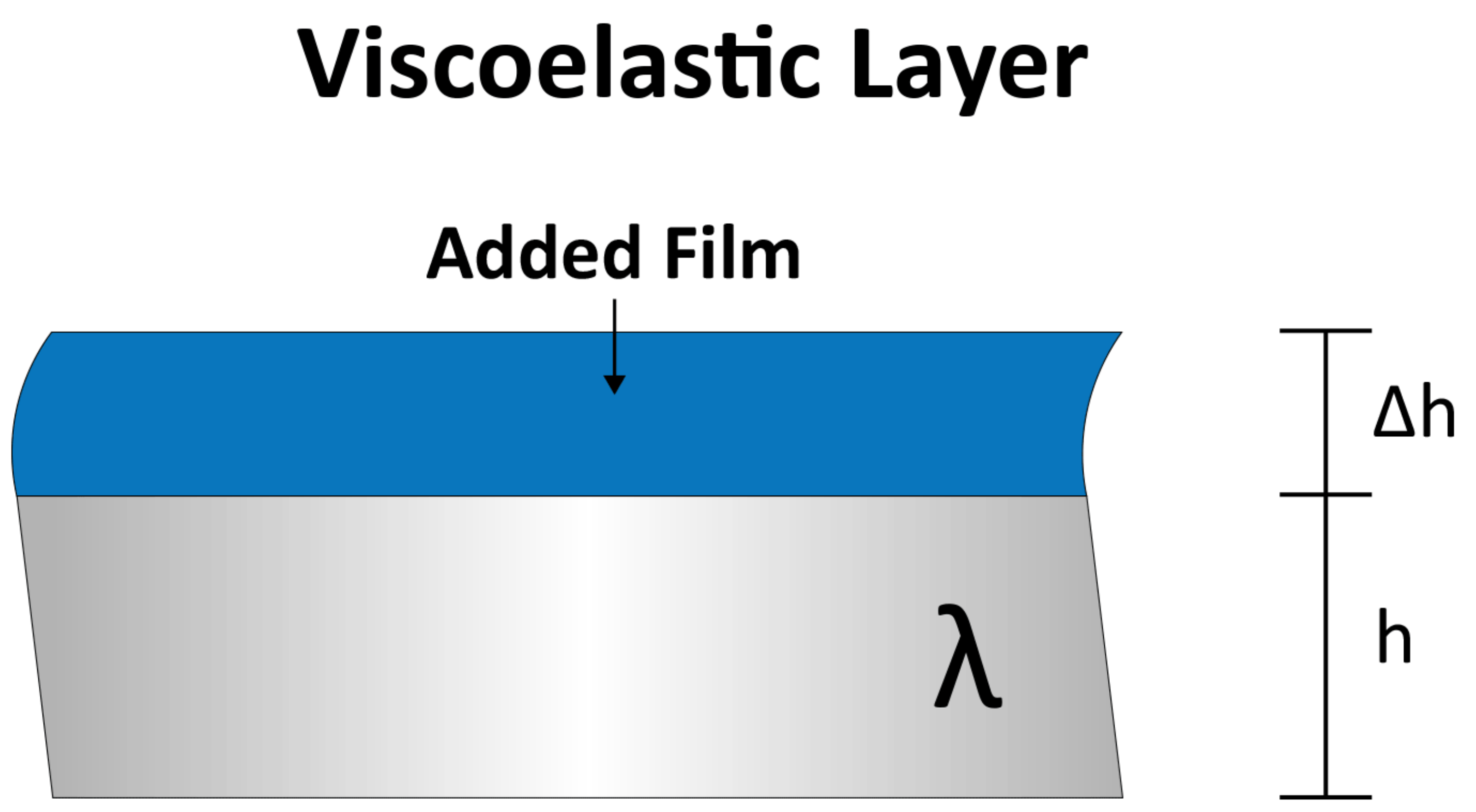
Quartz-Crystal Microbalance With Dissipation Monitoring

Rigid films move in sync and conserves energy

Viscoelastic film deforms independently and dissipates energy





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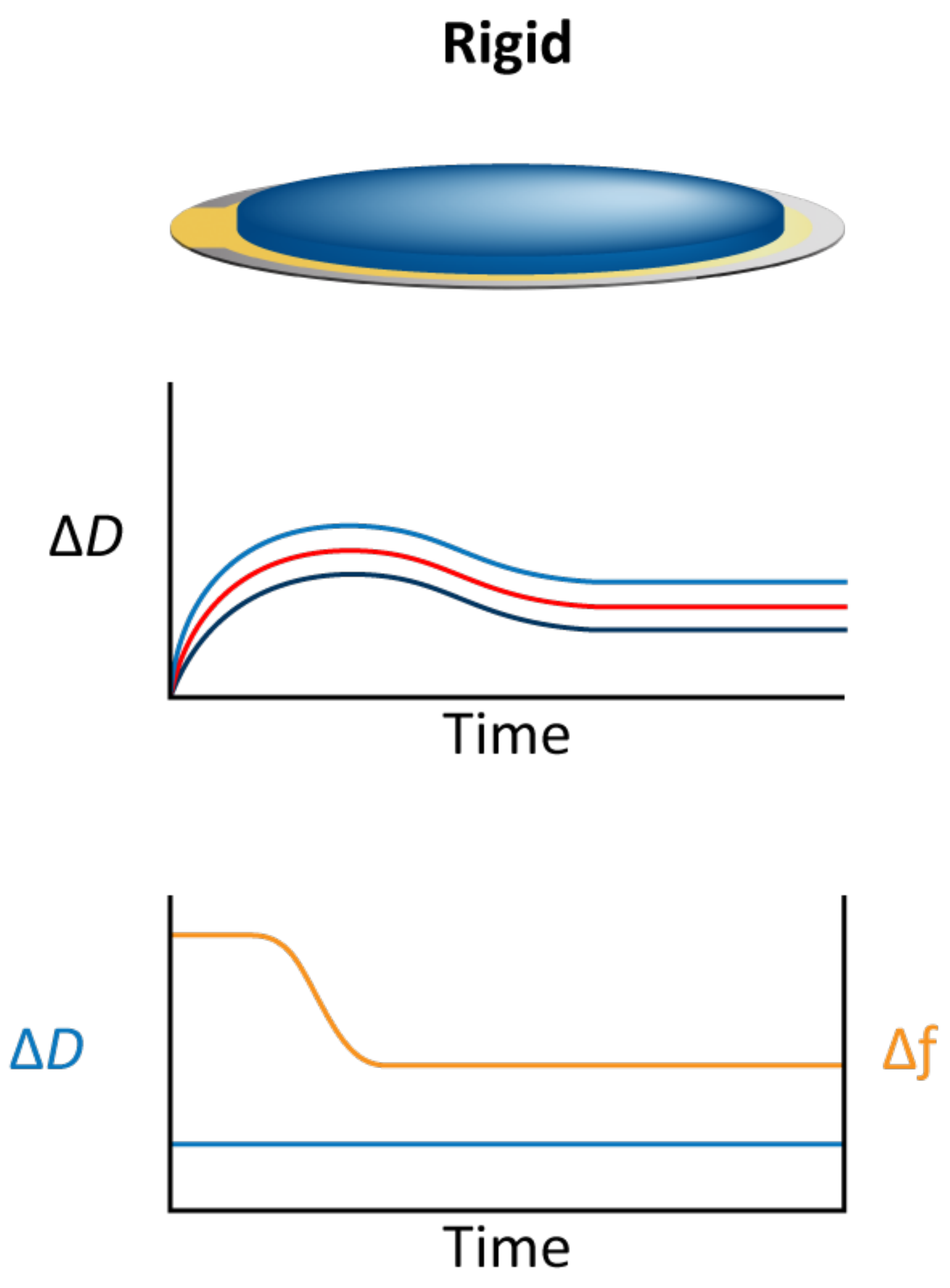
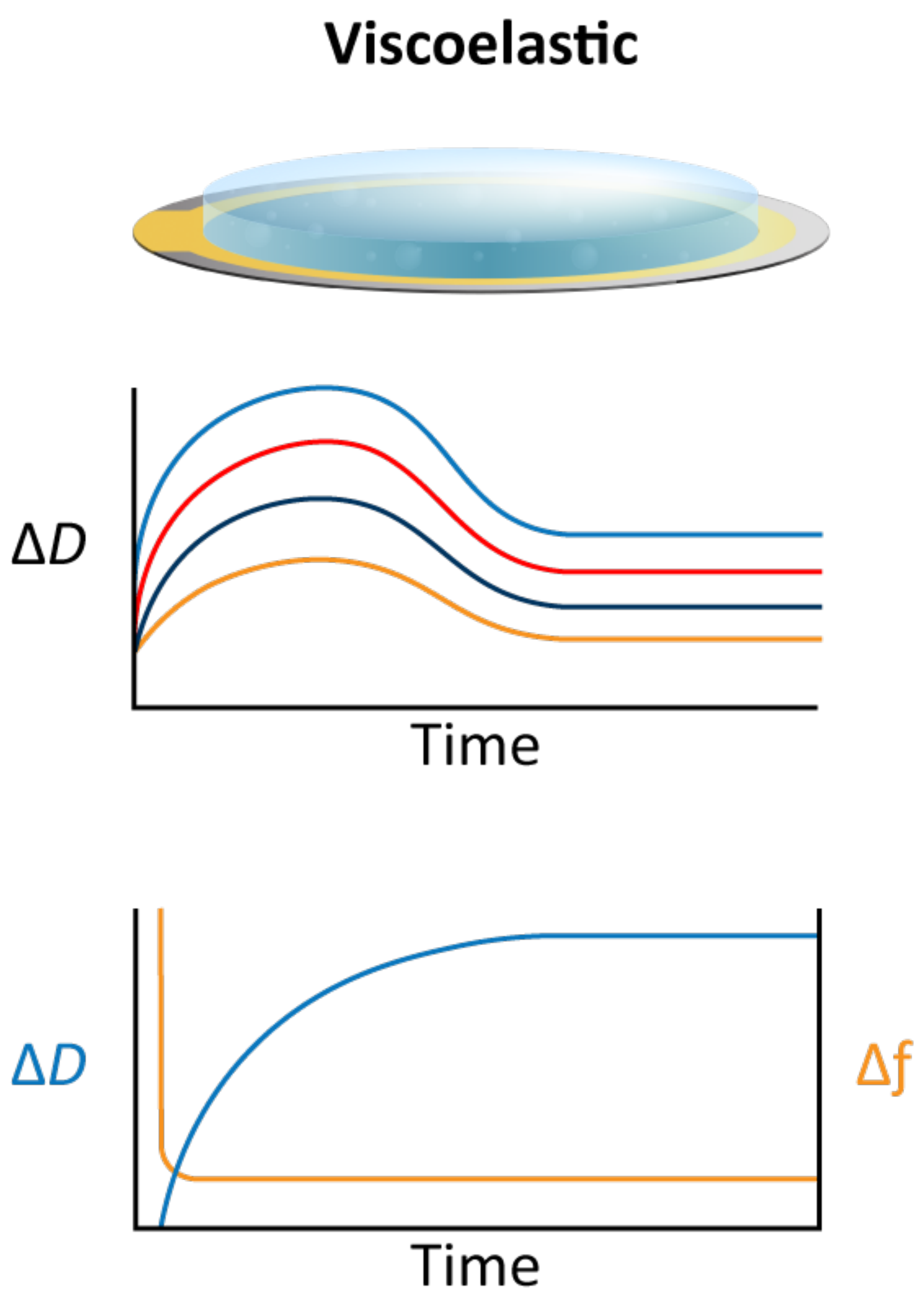
Multi-Harmonic Data Unlocks Mechanical Properties Characterization





Rigid layers show consistent ratios in frequency shifts with harmonic order

Viscoelastic films show increasing dissipation and nonlinear frequency behavior that varies with overtone

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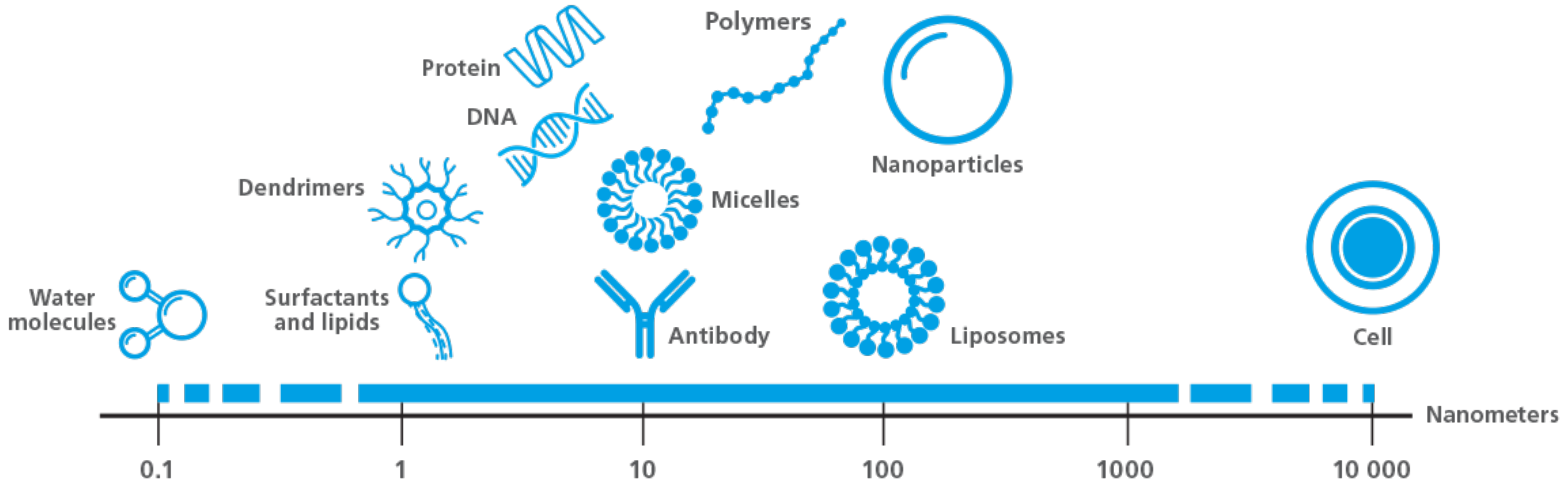
Pros and Cons of QCM-D

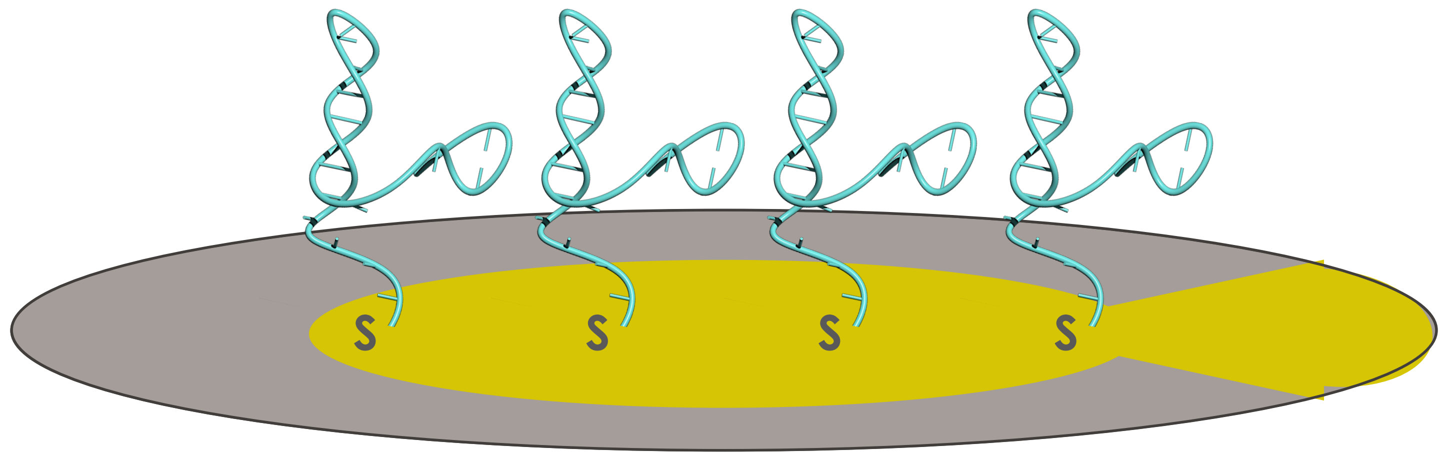
QCM-D can monitor viscoelastic behavior

Real-time kinetics of molecular assembly and adsorption

Sensitive to soft layers (proteins, polymers, etc.)

QCM-D monitors “wet mass” – mass + coupled water molecules – cannot separate





No direct thickness or refractive index of material

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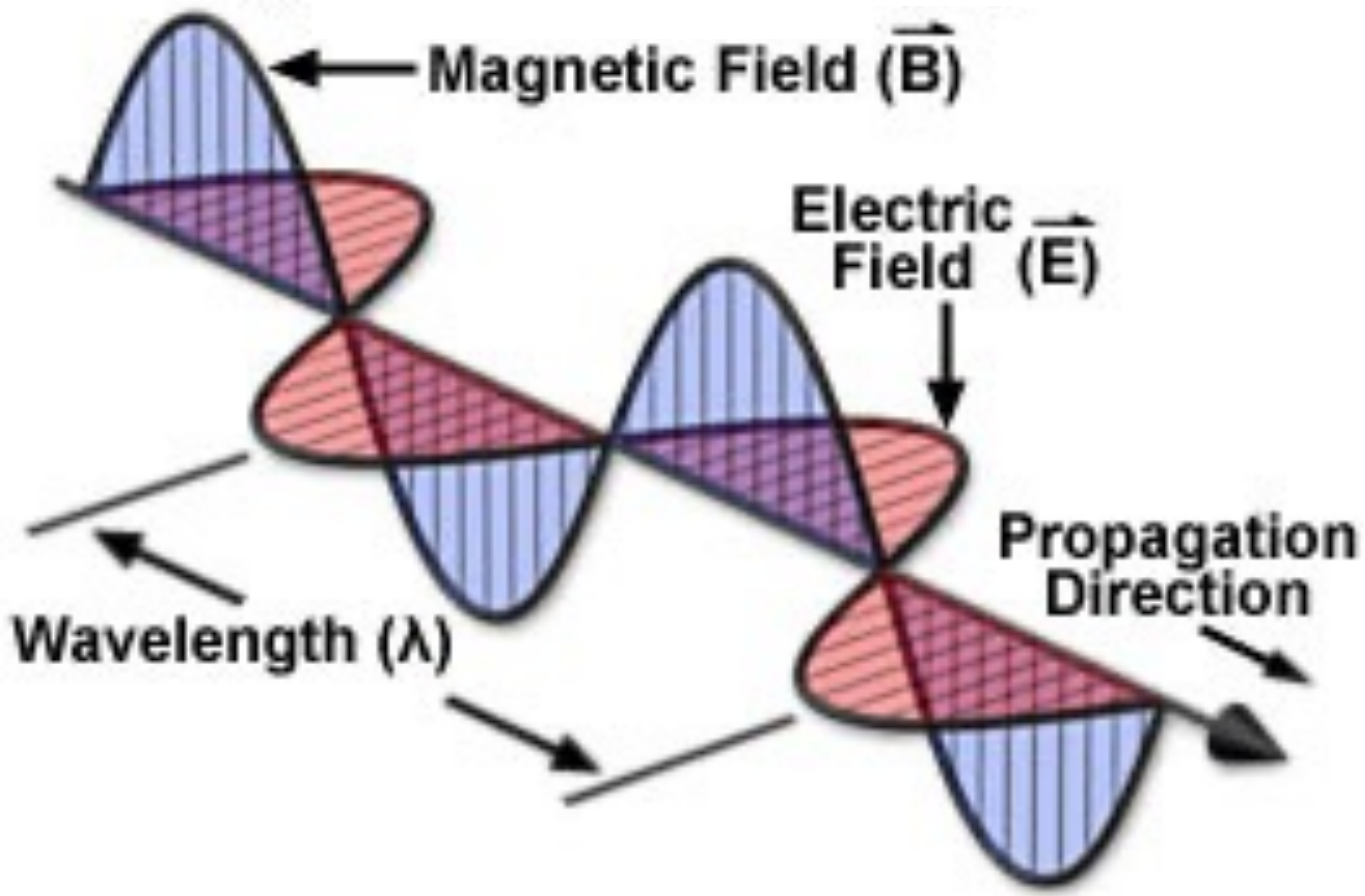
Key Takeaways

- QCM-D is a versatile technique with detection range from 1 Å to 1 µM
- Piezoelectric quartz leads to change in frequency of oscillation = mass
- Monitoring dissipation provides viscoelastic properties of layer
- Characterizing rigid vs. viscoelastic films

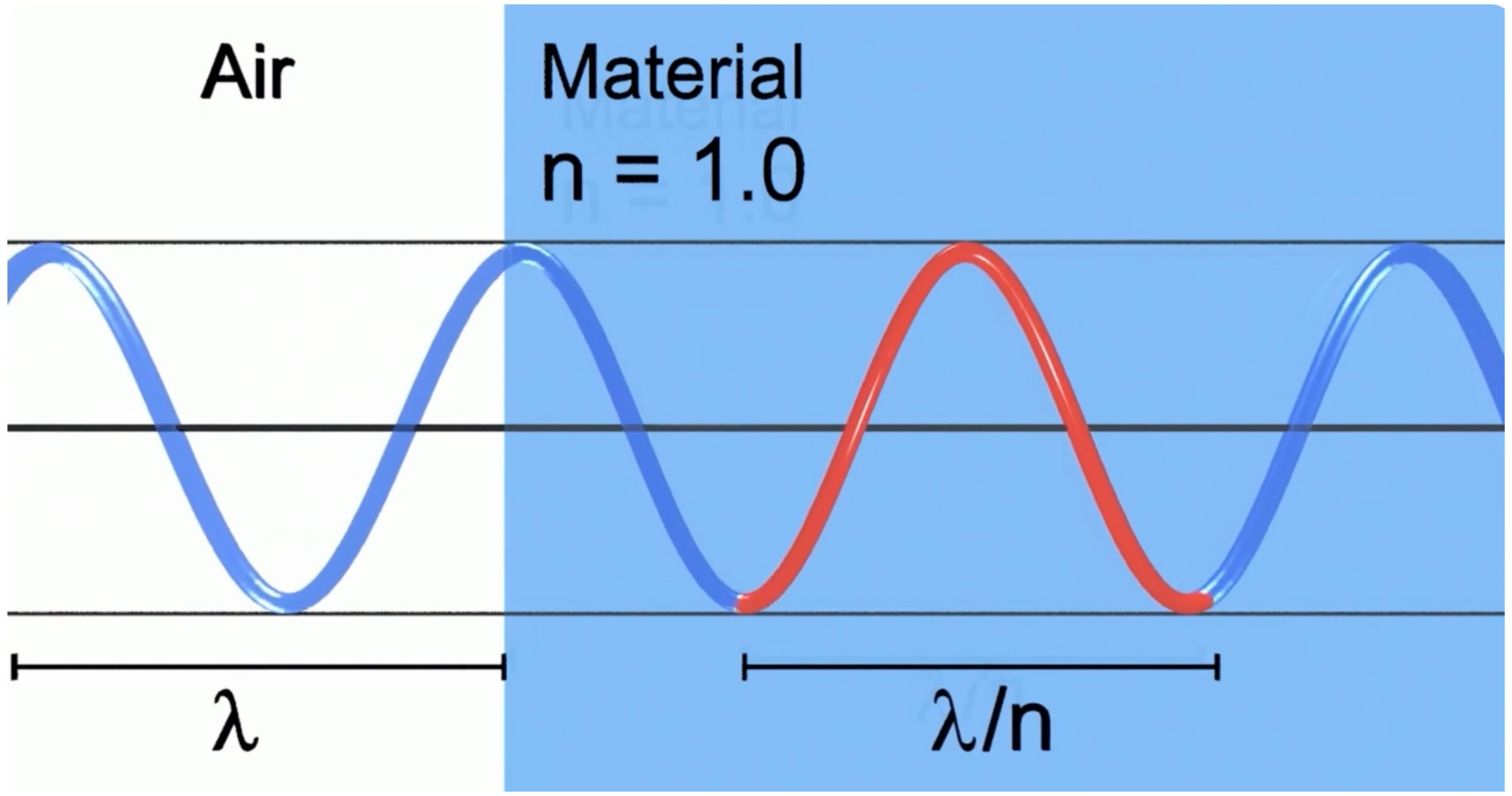
How can we characterize absolute film thickness and optical properties?

Basic Principles of Light Propagation Through Materials

Light as an oscillating electromagnetic field



Continuous propagation through material when refractive index = 1

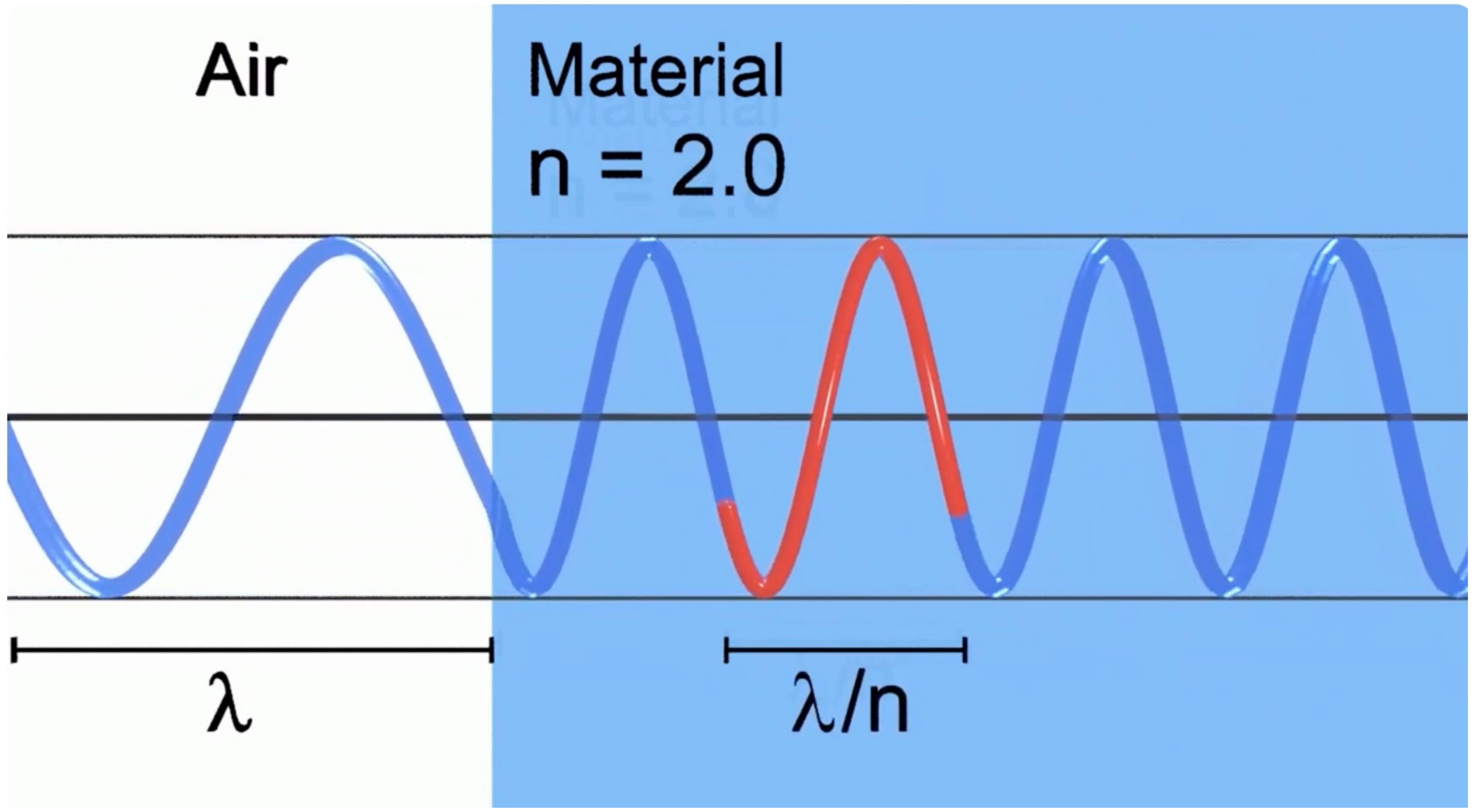


$$n = \frac{c}{v}$$

Image credit: Hiroyuki Fujiwara

Basic Principles of Light Propagation Through Materials

If refractive index increases, wavelength of light becomes shorter due to the light electric field and material



Continuous propagation through material when refractive index = 1

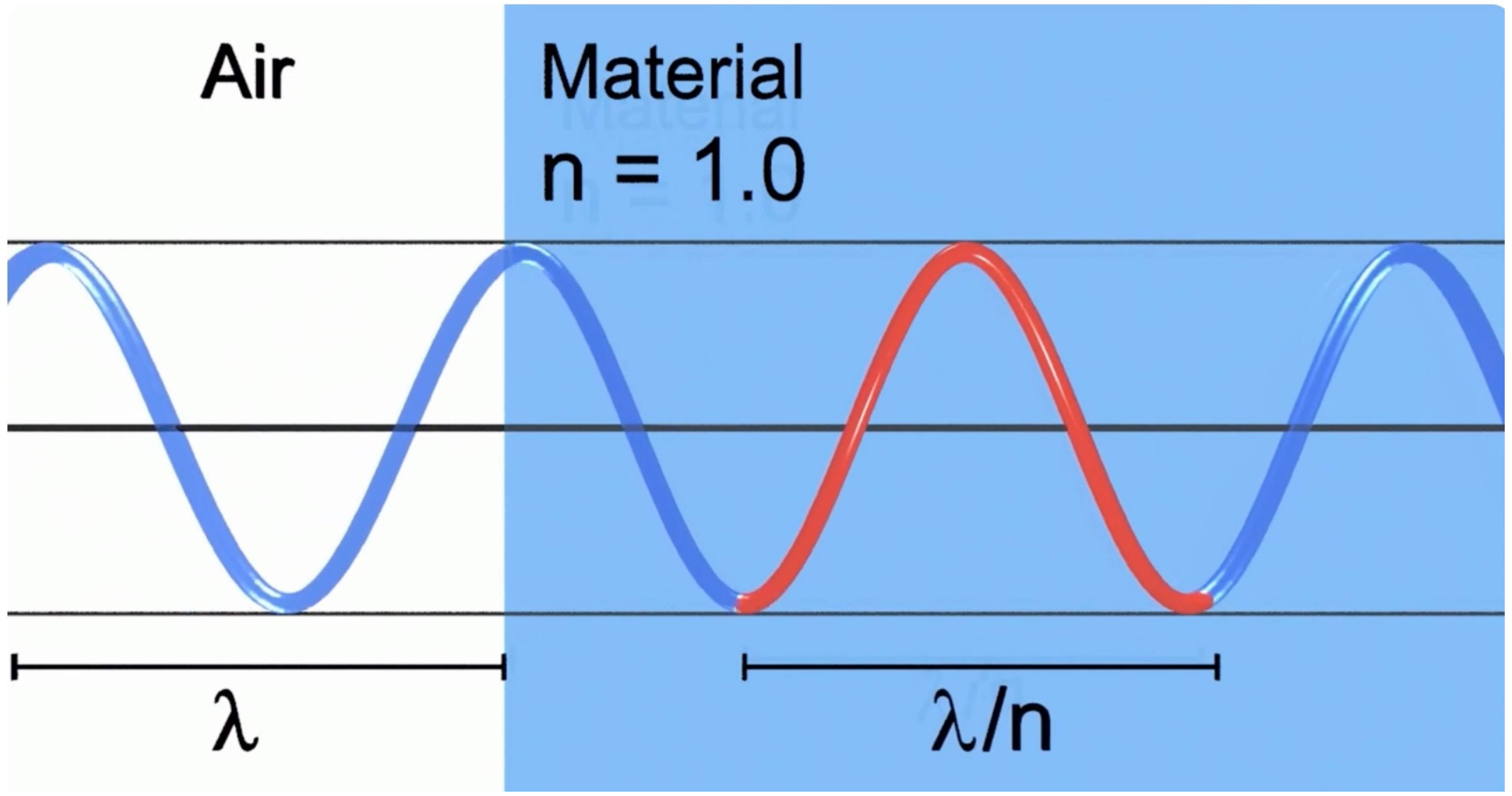


Image credit: Hiroyuki Fujiwara

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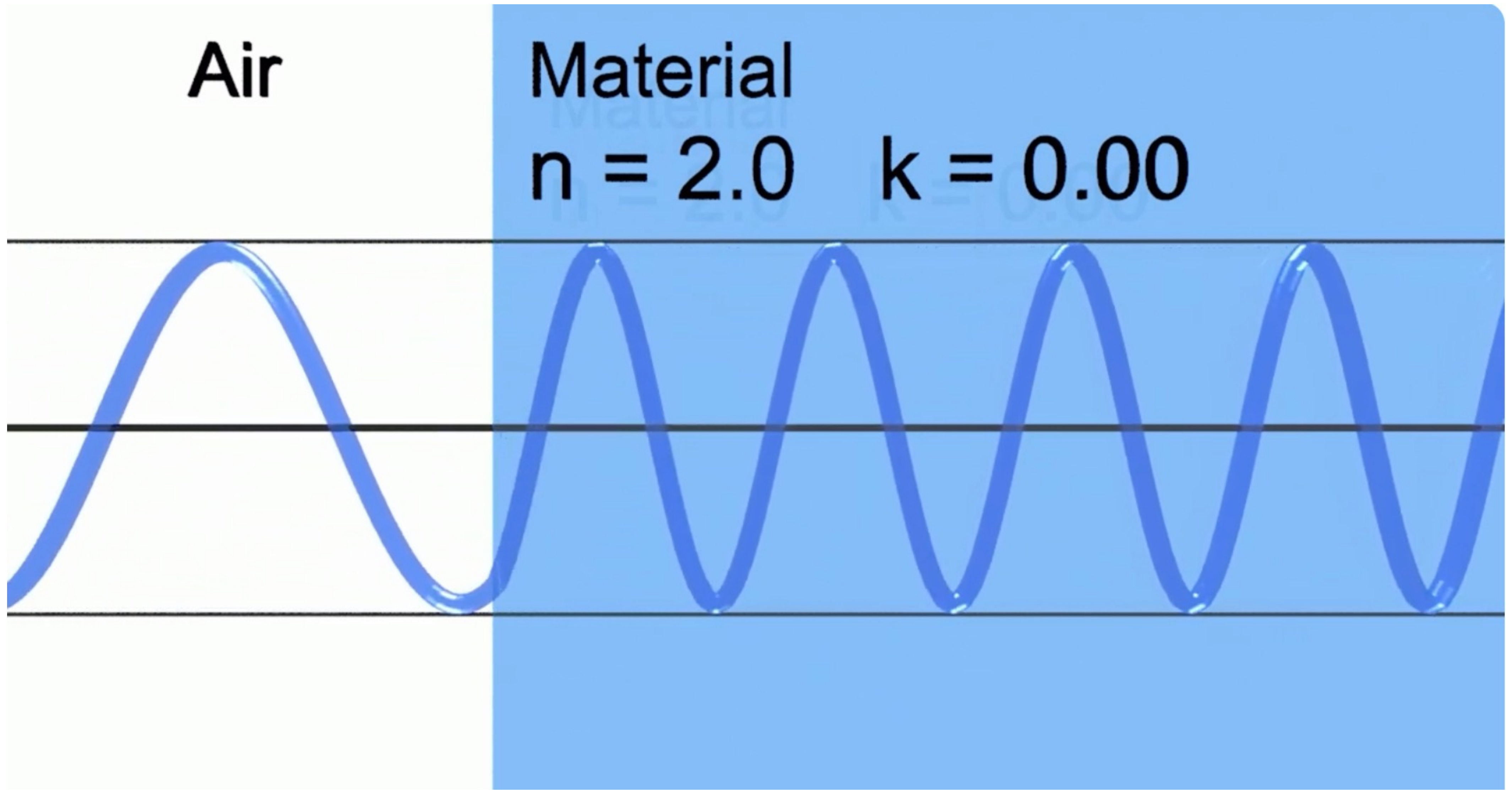
Basic Principles of Light Propagation Through Materials

Extinction coefficient (k) = 0

Material completely transparent

No change in amplitude



Increase k

Amplitude of wave decreases based on light absorption in material

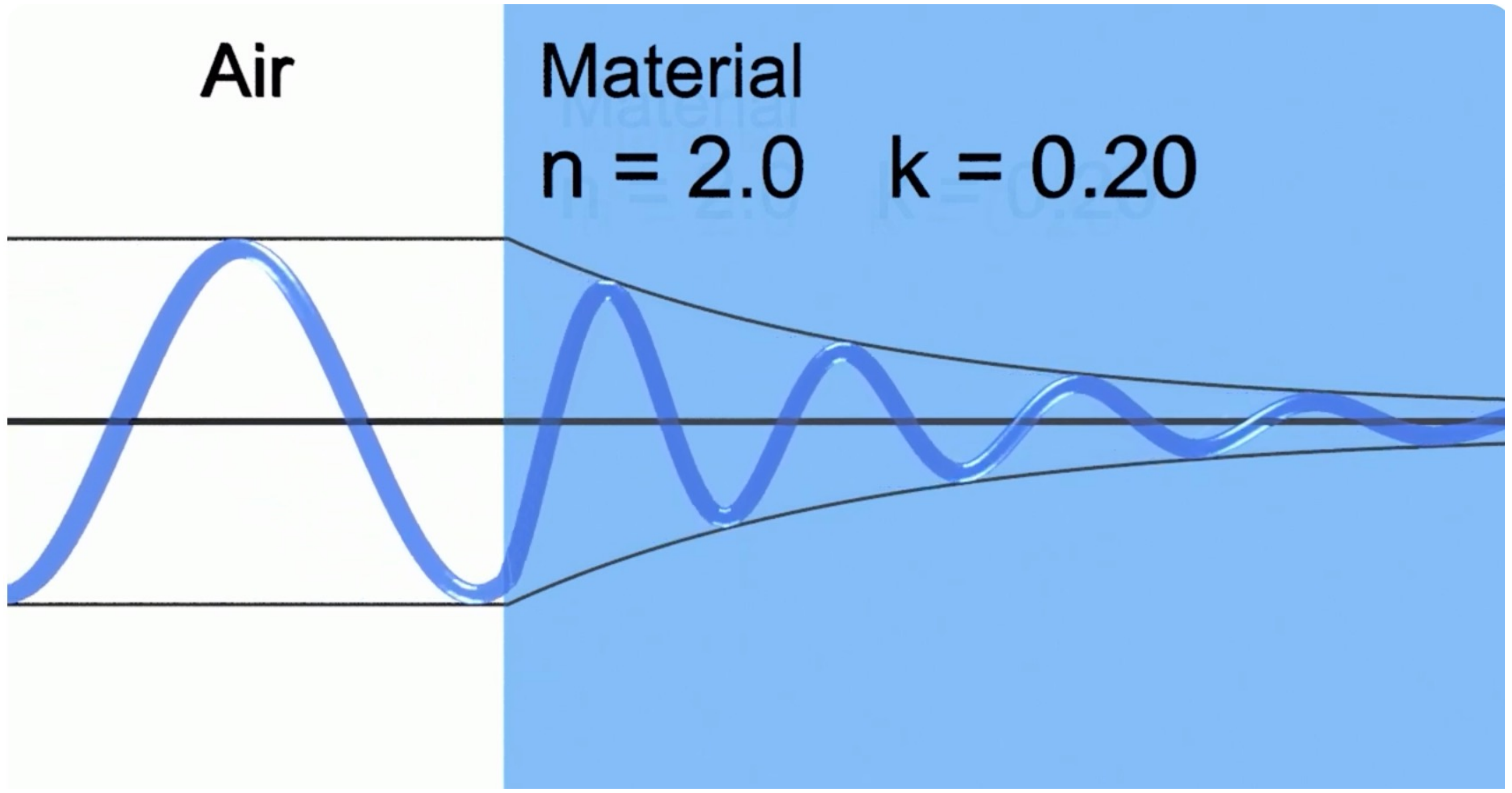


Image credit: Hiroyuki Fujiwara

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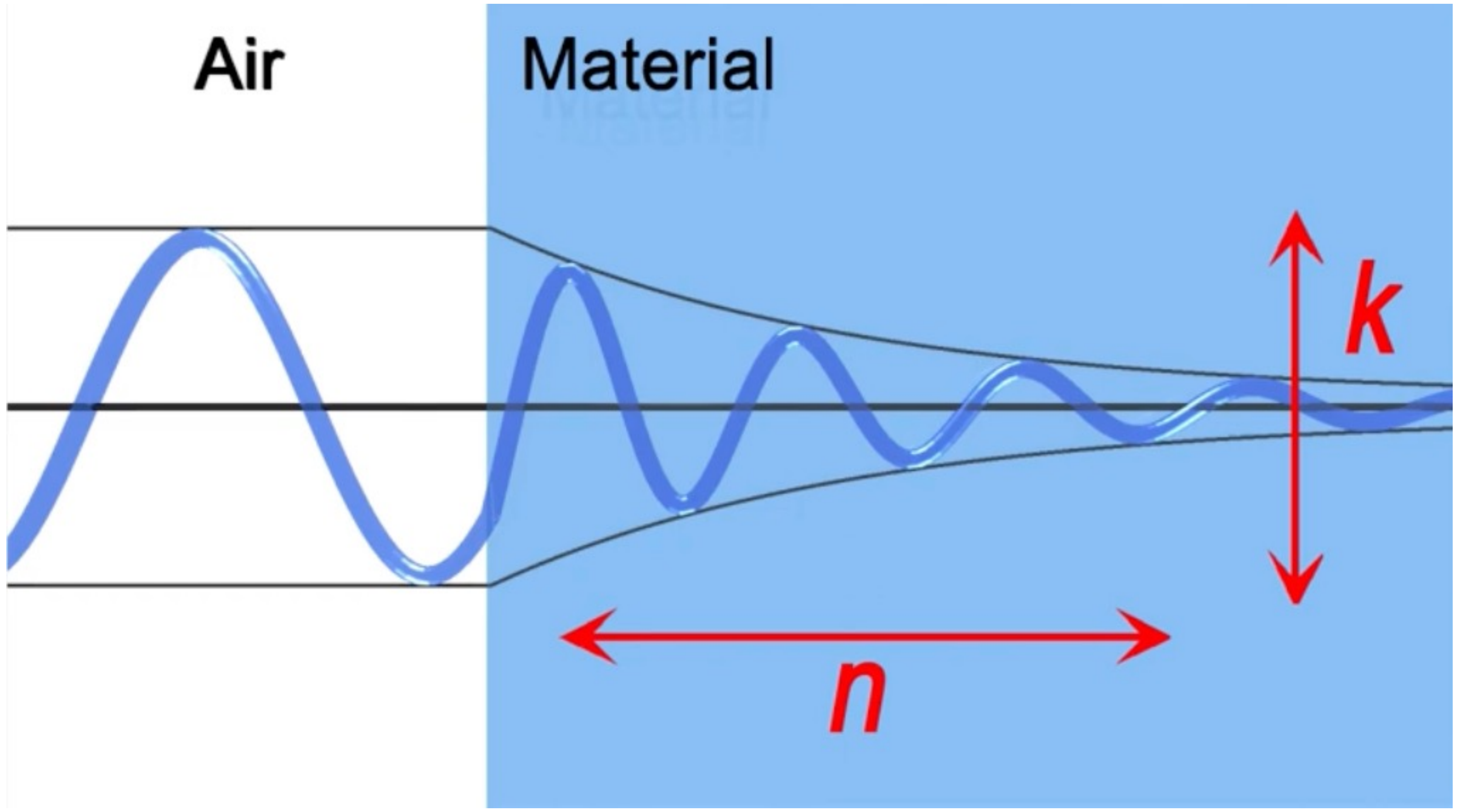
Optical Constants n & k Define Material Optical Properties



Absorption coefficient

$$\alpha = \frac{4\pi}{\lambda} k$$

Ellipsometry is an optical instrument that determines the optical constant of materials

Image credit: Hiroyuki Fujiwara

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Ellipsometry Shines Polarized Light onto Surfaces

Linearly polarized light (s and p components oscillate in phase)

Reflected light shows a different polarization state

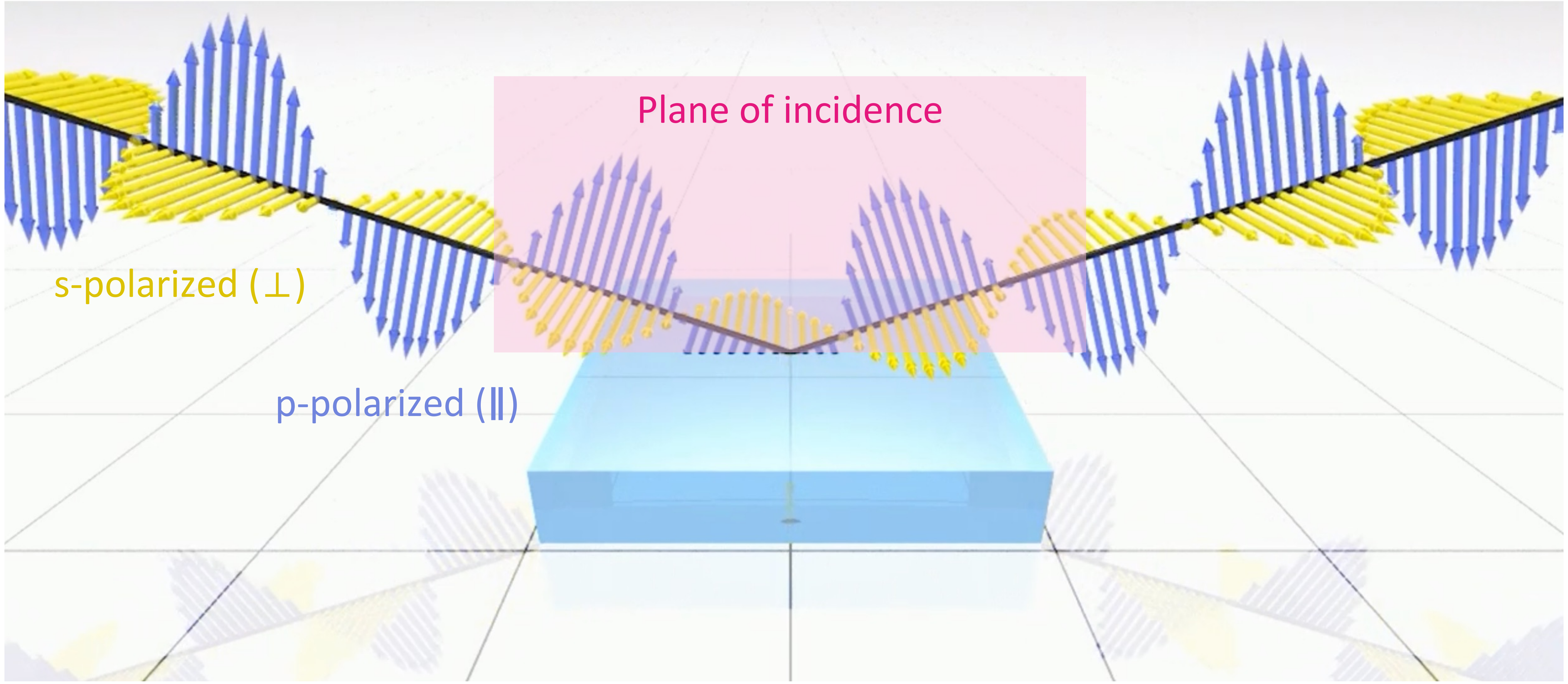

Image credit: Hiroyuki Fujiwara

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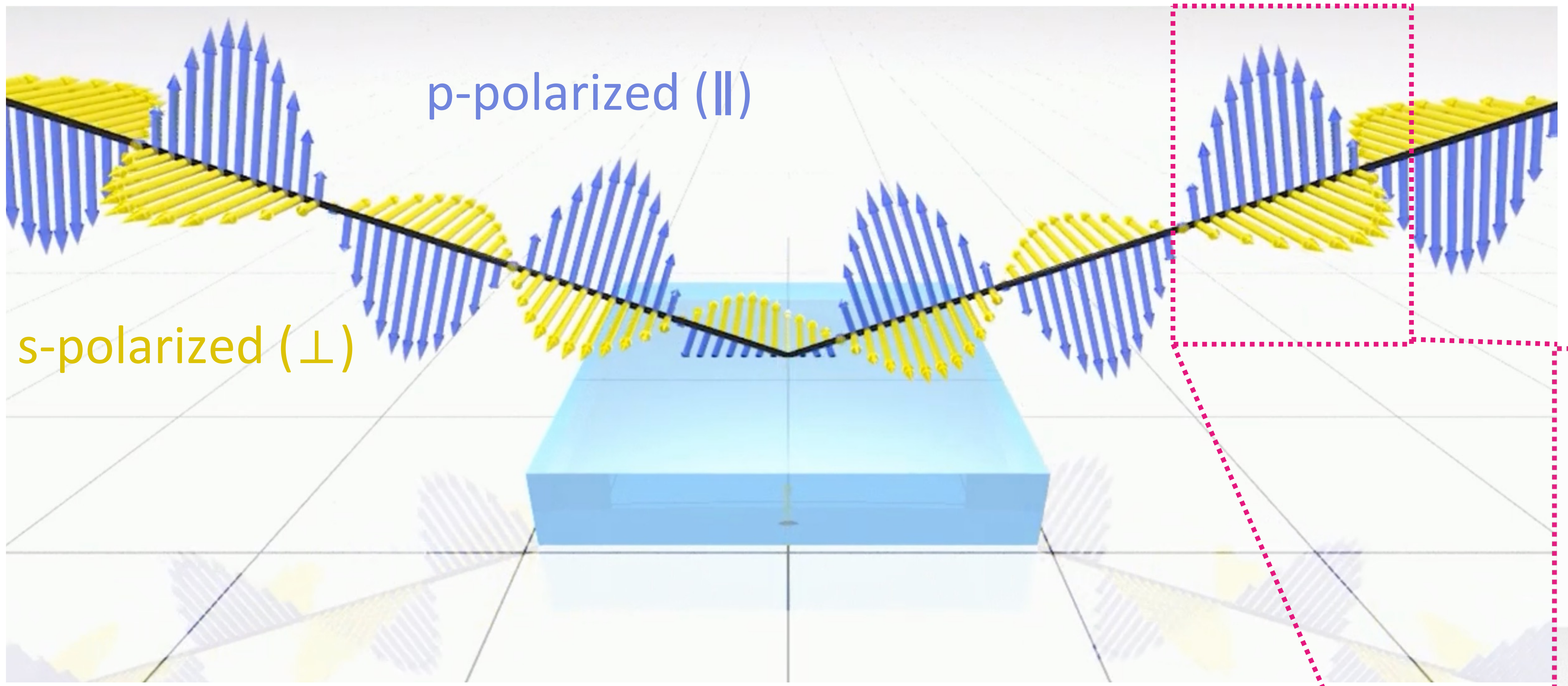
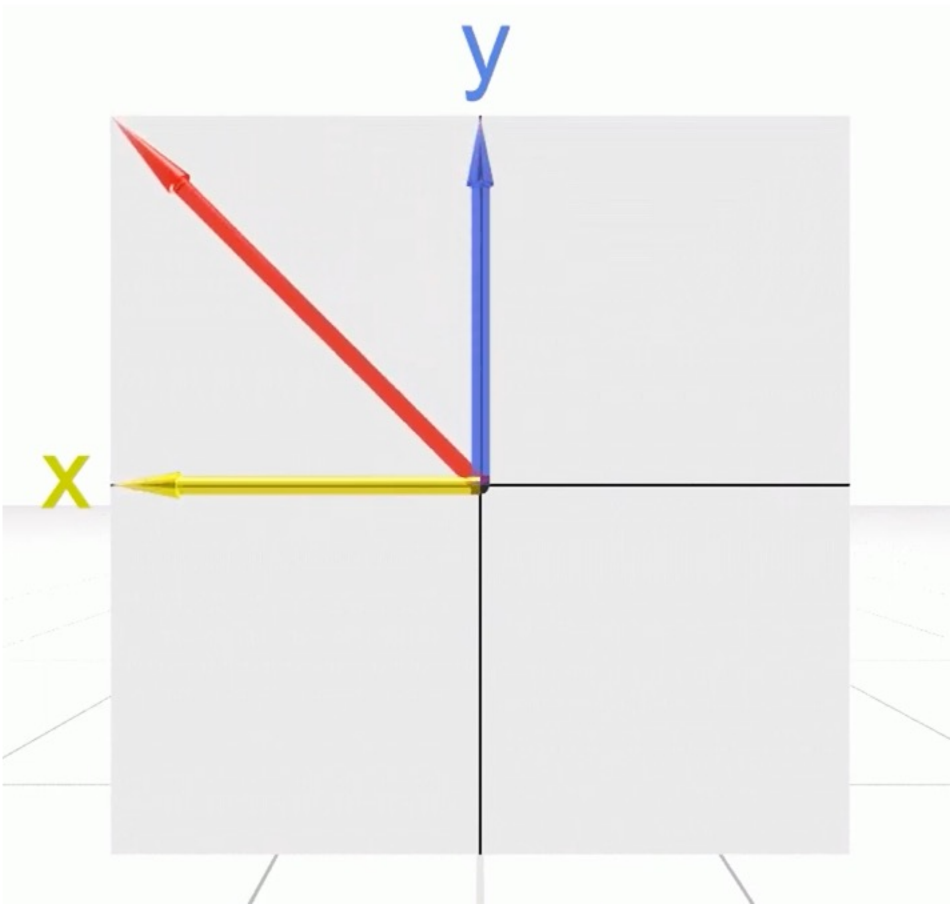
Oscillation of Electric Field Components



Adding electric field components in x-y directions forms a synthesized vector that oscillates linearly



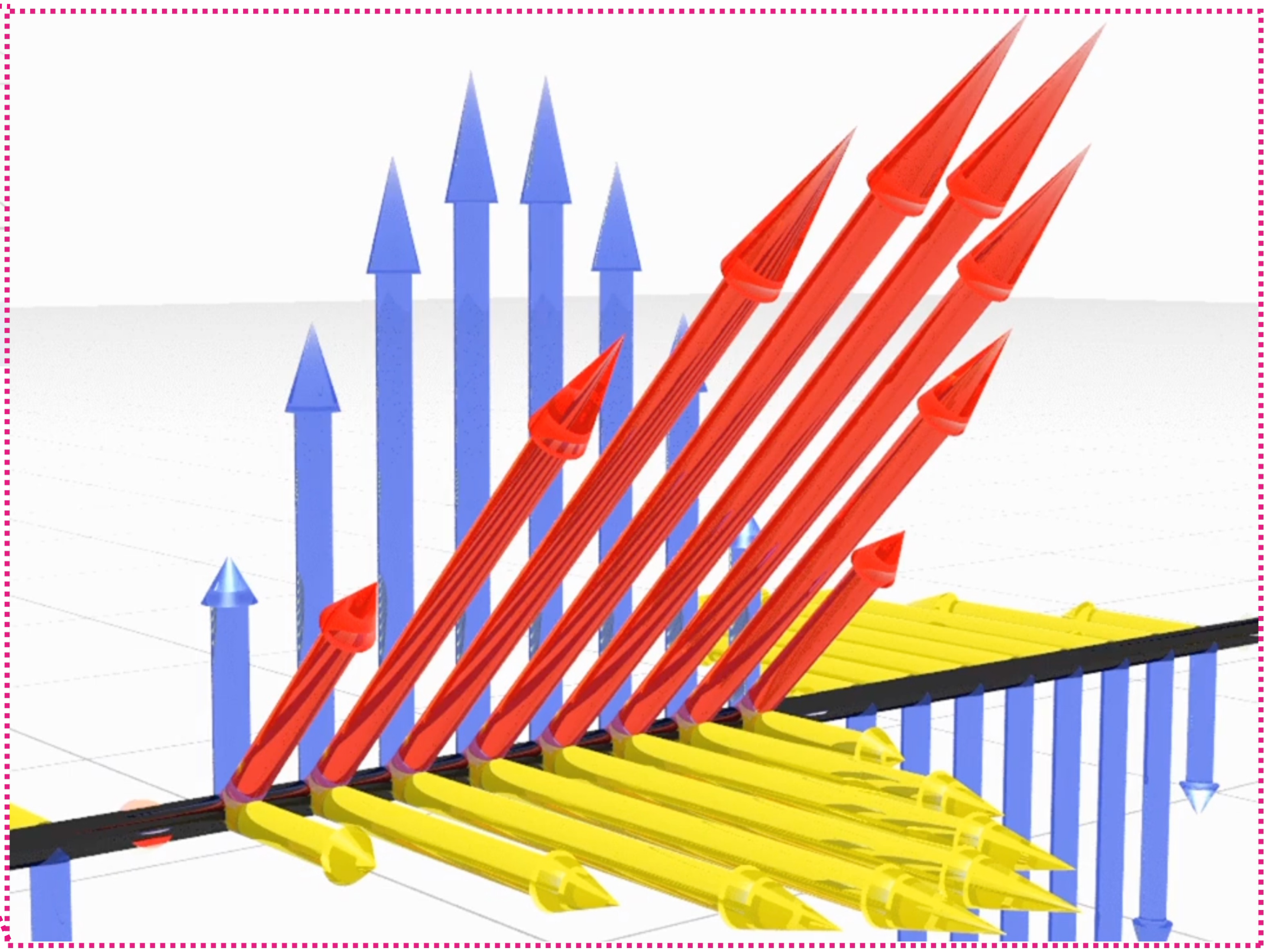


Image credit: Hiroyuki Fujiwara

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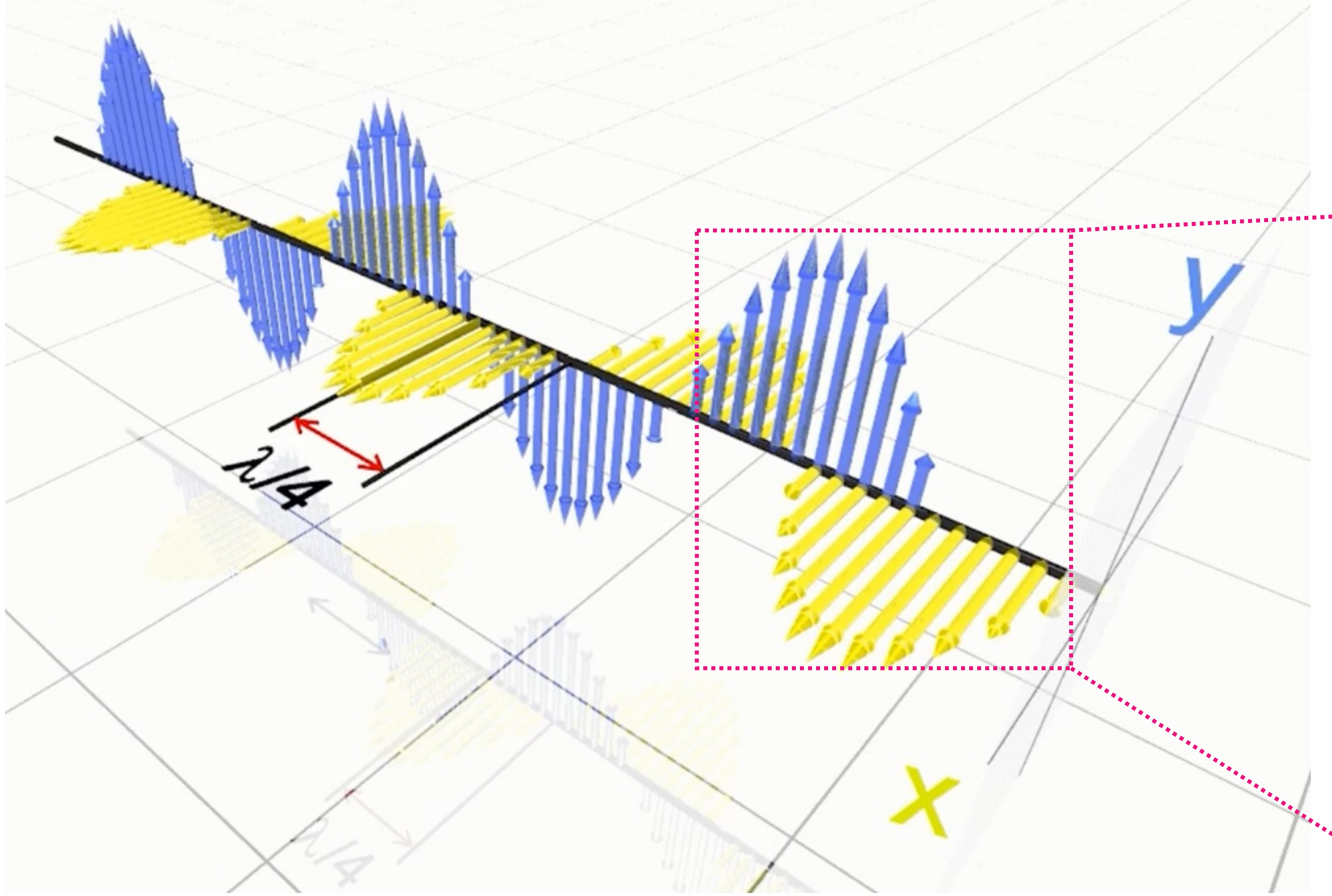
Phase Shifts Causing Changes in Combined Vector

Consider wave in the x-direction advances forward compared to the y-direction with a phase difference (90°)



Superimpose waves in x-y direction – synthesized vector rotates continuously on x-y plane as light propagates

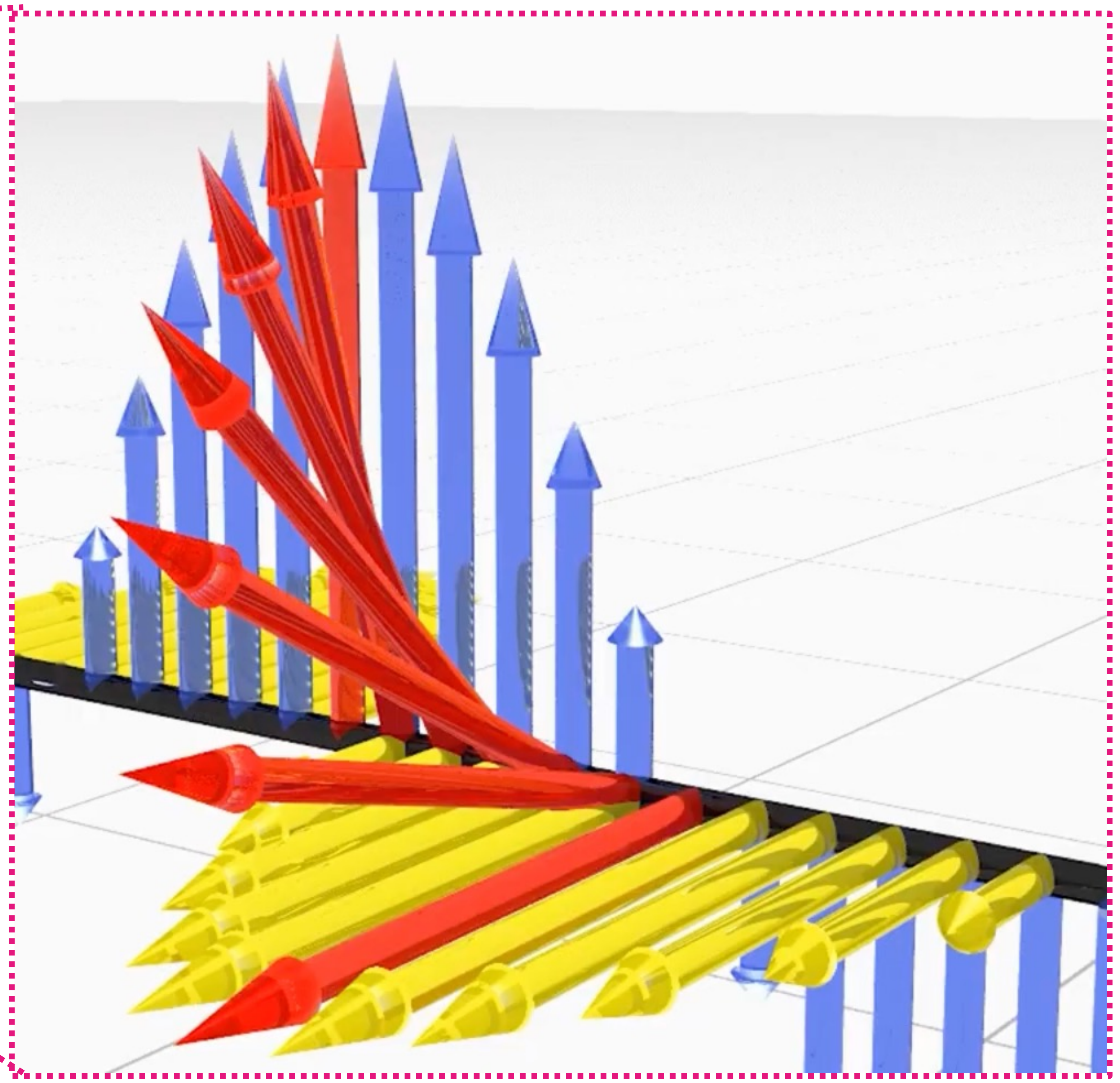
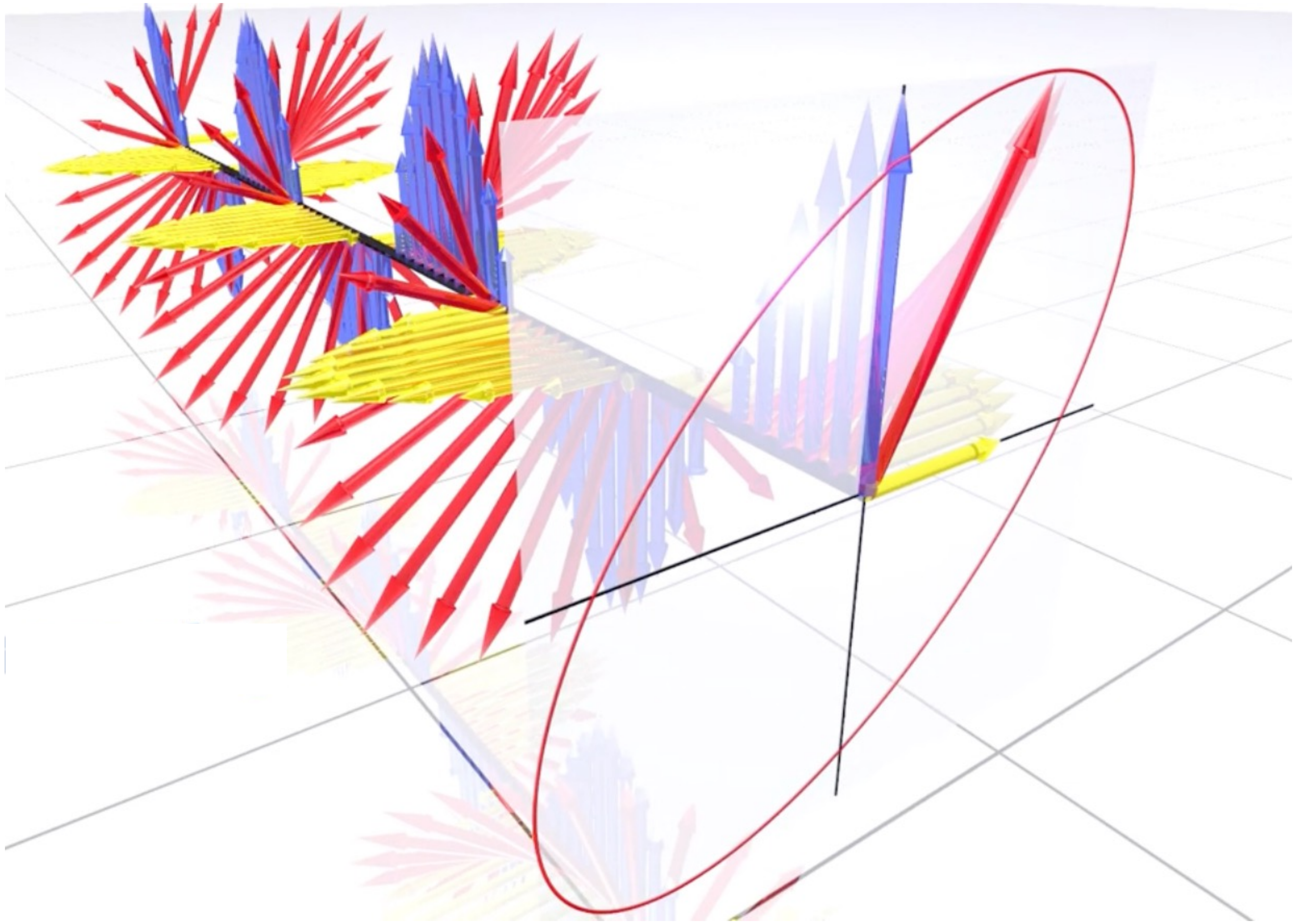
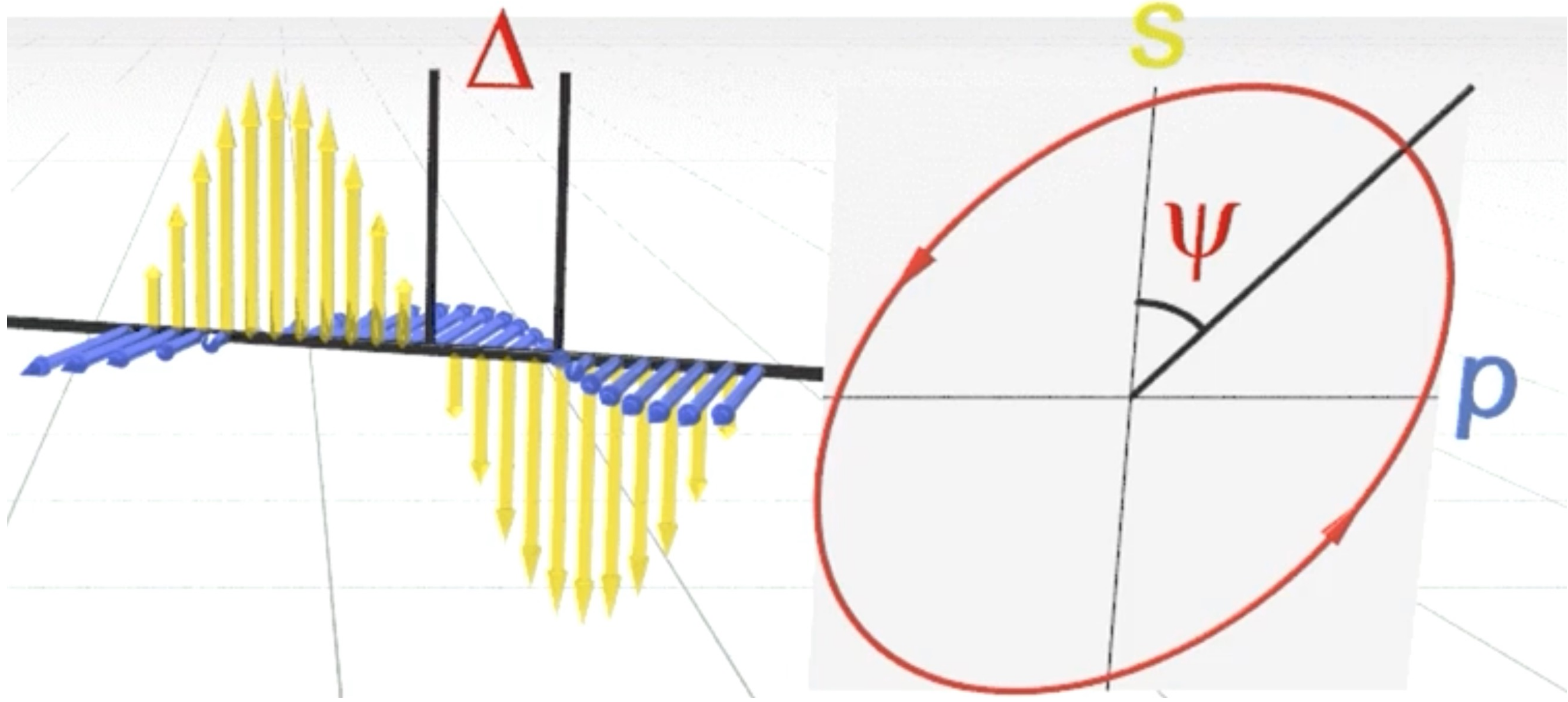


Image credit: Hiroyuki Fujiwara

“Ellipsometry” – Light Polarization Often Elliptical



Ellipsometry measures two angles:
Δ and Ψ of the reflected light



Δ: relative phase difference between s and p polarizations

Ψ : angle determined by relative amplitude of s and p waves

Optical constants “n” and “k” determined from Δ and Ψ

Image credit: Hiroyuki Fujiwara

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"Ellipsometry" – Light Polarization Often Elliptical

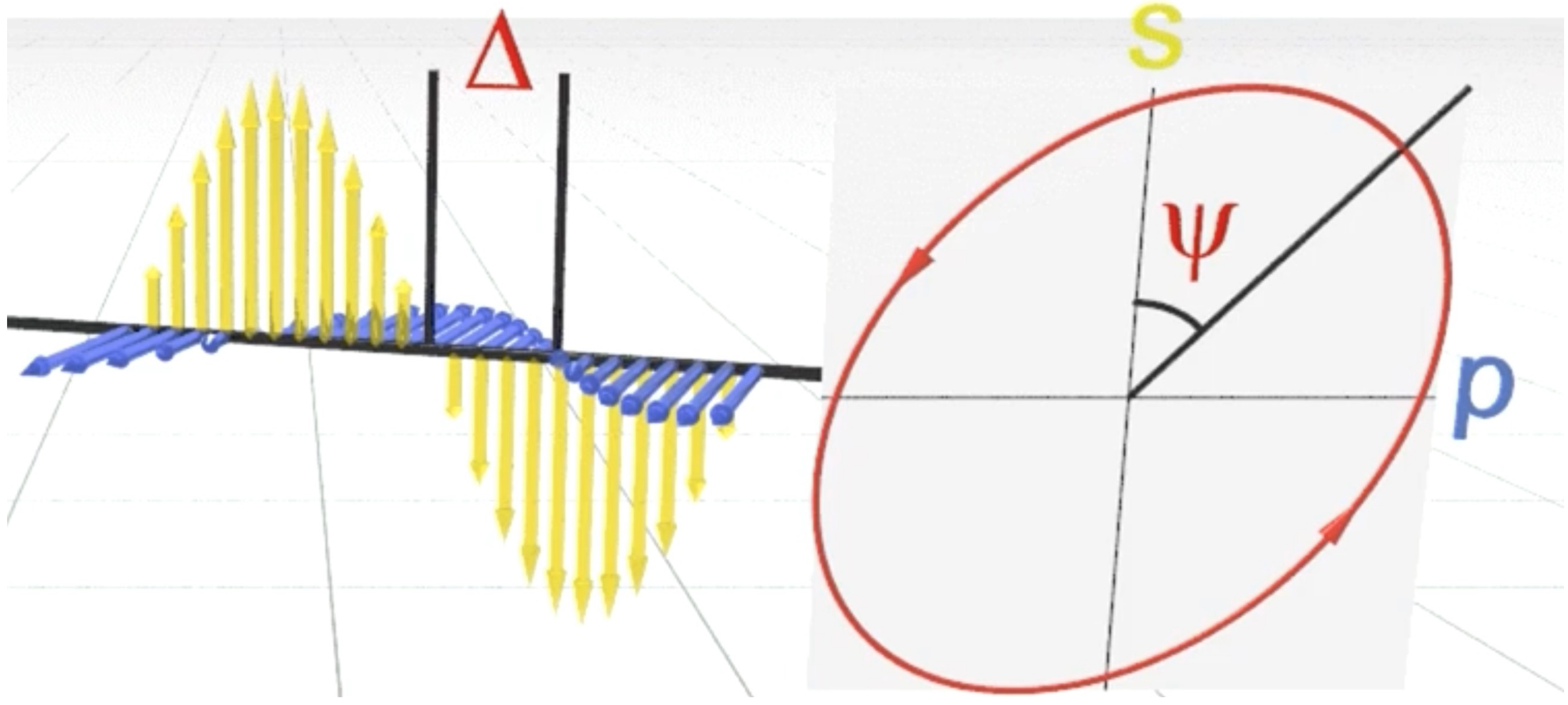
Complex ratio of reflection coefficients of p and s polarized light

$$\frac{R_p}{R_s} = \tan\Psi e^{i\Delta}$$

↓

Refractive index (n)
Extinction coefficient (k)
Thickness of the film

Ellipsometry measures two angles:
Δ and **Ψ** of the reflected light



Δ: relative phase difference between s and p polarizations

Ψ : angle determined by relative amplitude of s and p waves

Image credit: Hiroyuki Fujiwara

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Pros and Cons of Ellipsometry

Quantification of thin film thickness (~0.5–200 nm)

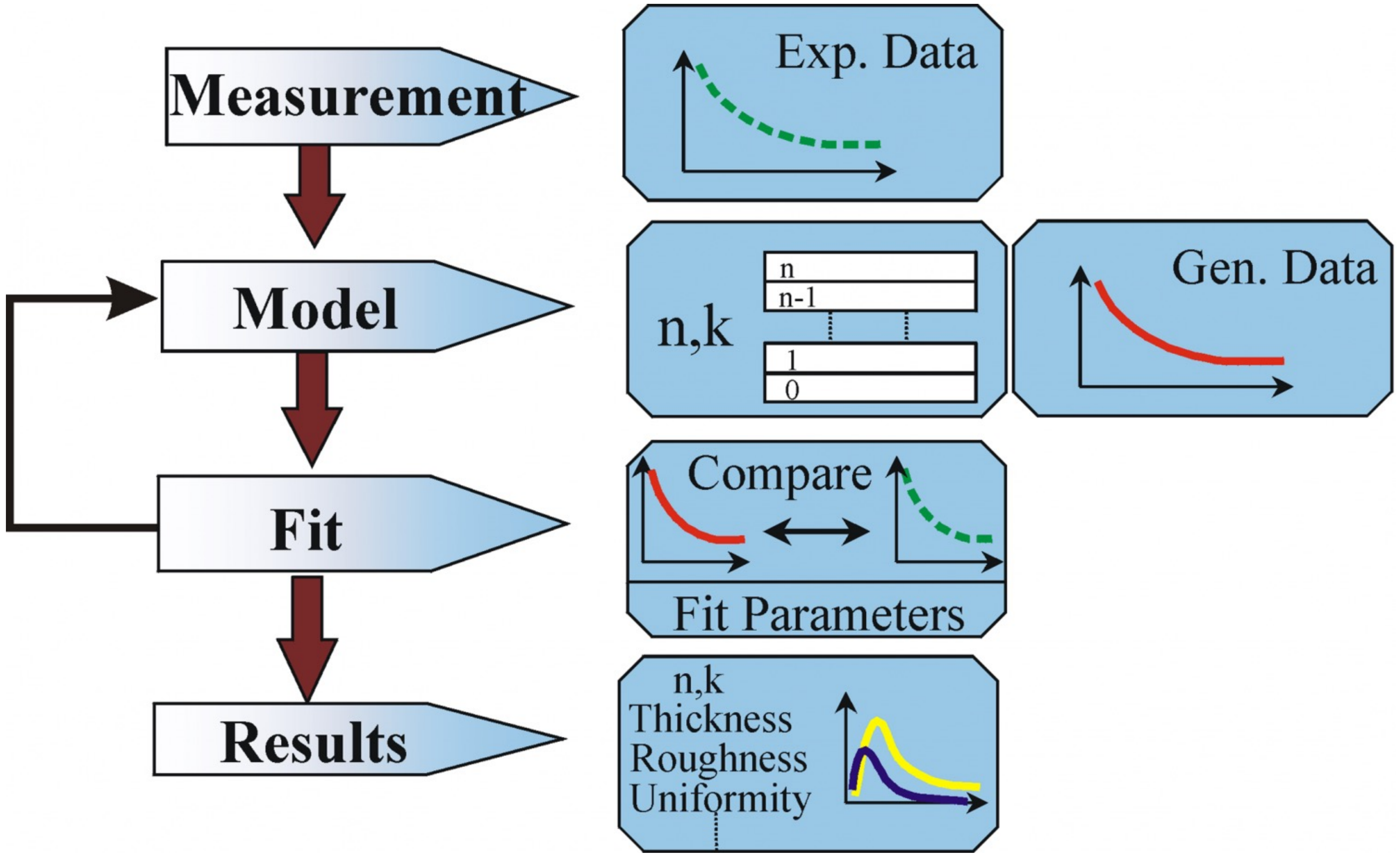
Complements QCM-D by providing dry mass and thickness

Provides refractive index – density, swelling, composition changes

Requires modeling to convert raw data to thickness

Needs uniform, smooth surfaces

Slow acquisition speed – cannot conduct fast kinetics

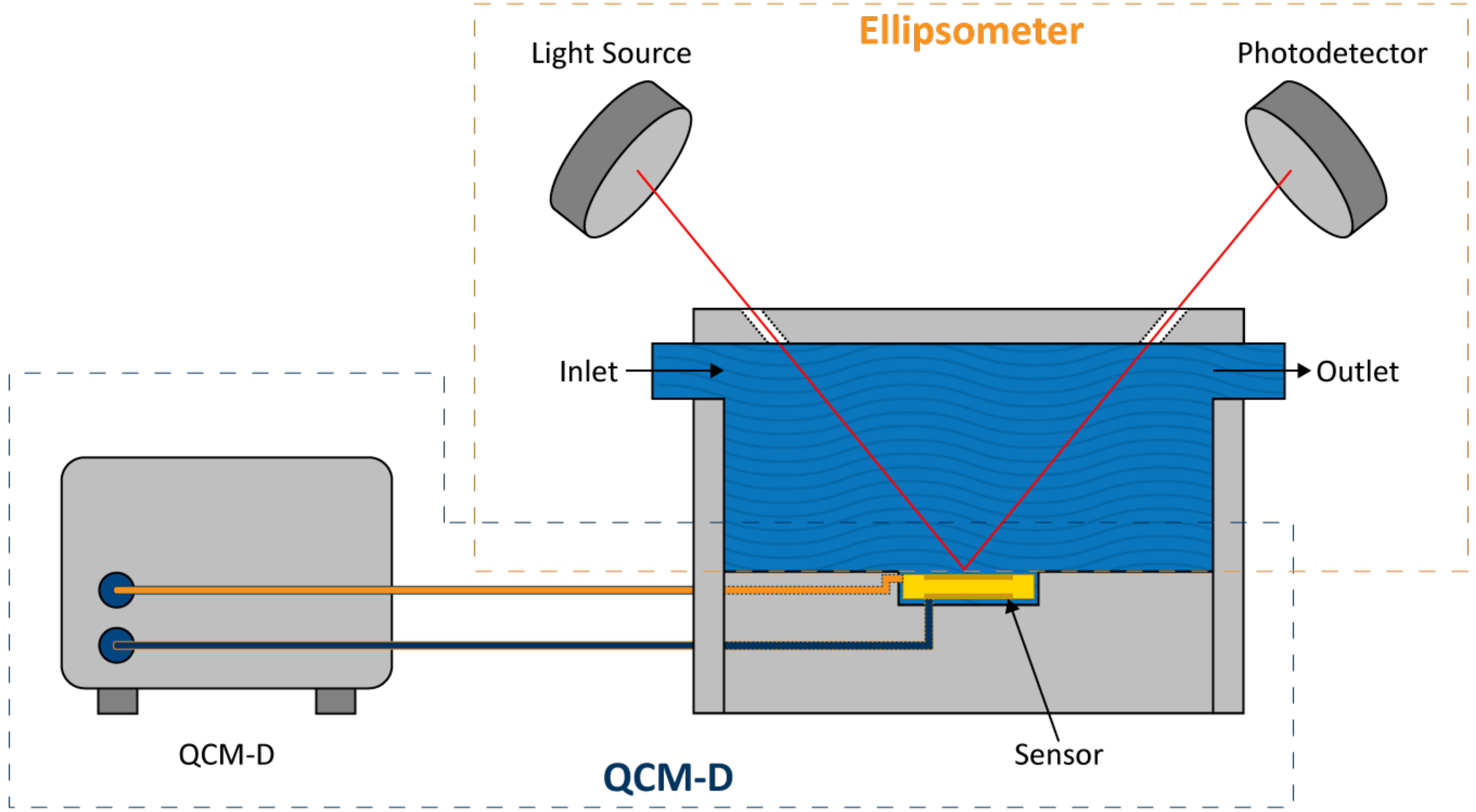


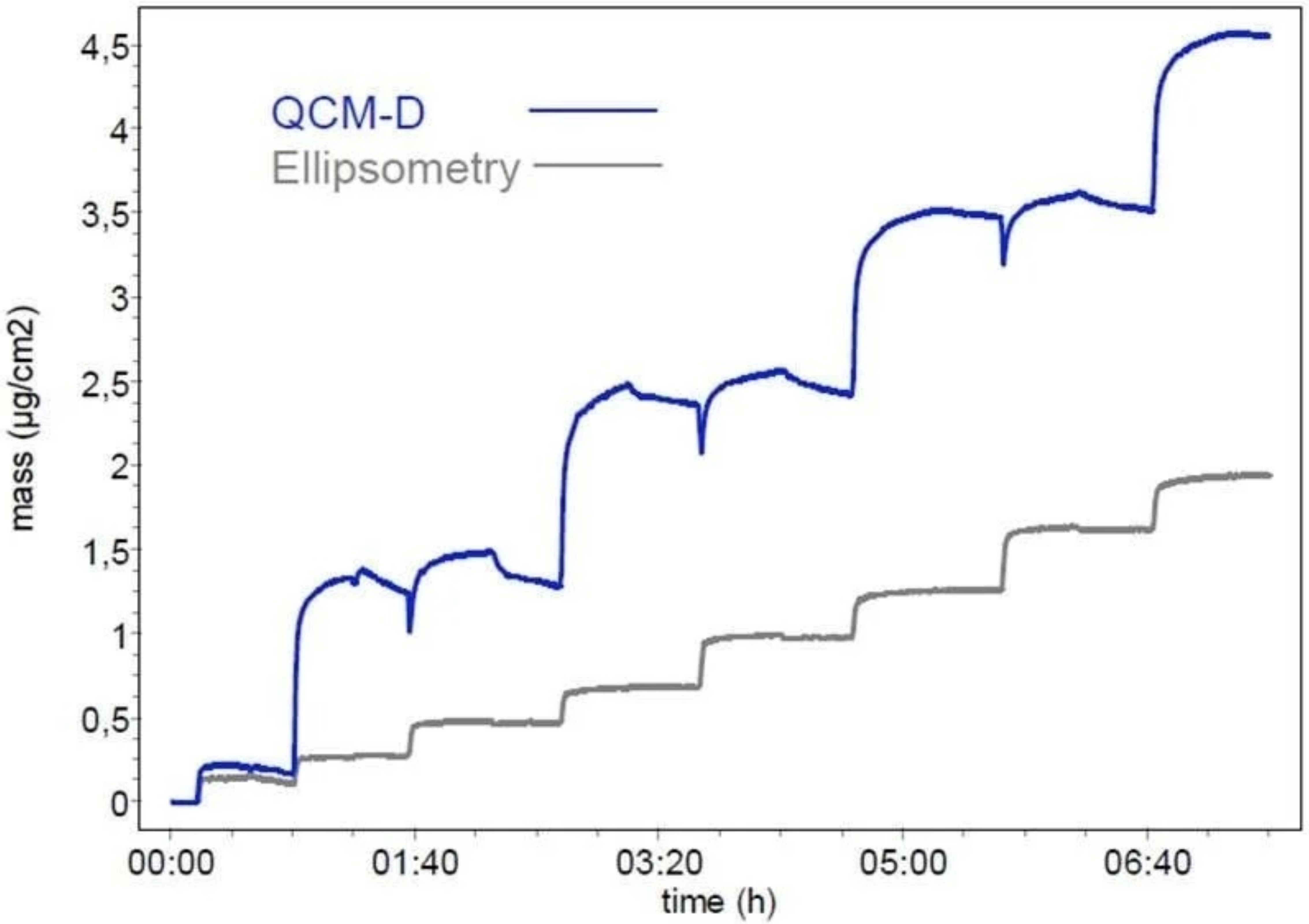
J.A. Woollam CHEMINA

Combinatorial Measurements: QCM-D + Ellipsometry

QCM-D measures real-time mass changes and viscoelastic properties at surfaces

Ellipsometry measures changes in the polarization of reflected light to determine film thickness, refractive index, and optical properties





Combinatorial Measurements: QCM-D + Ellipsometry

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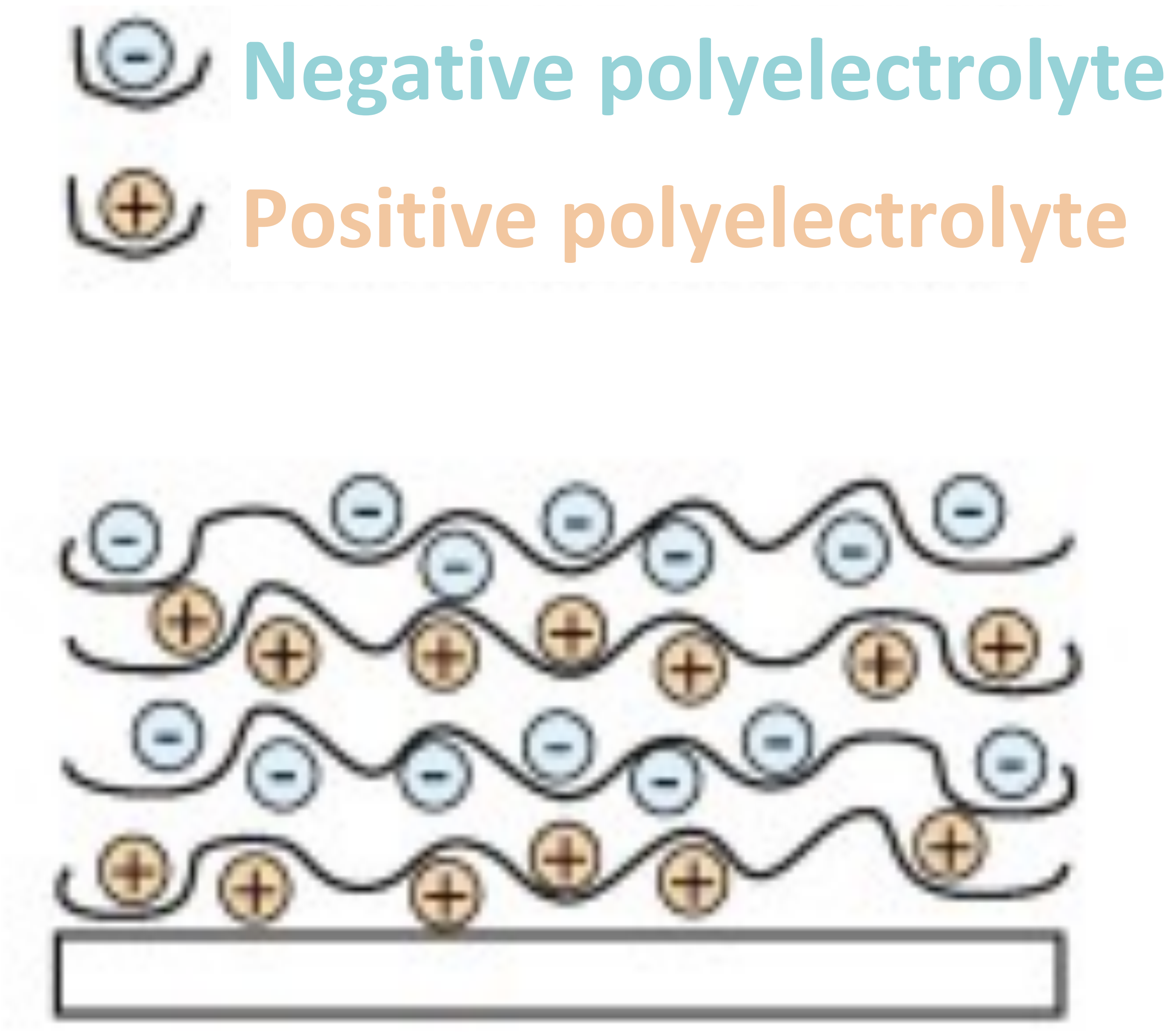
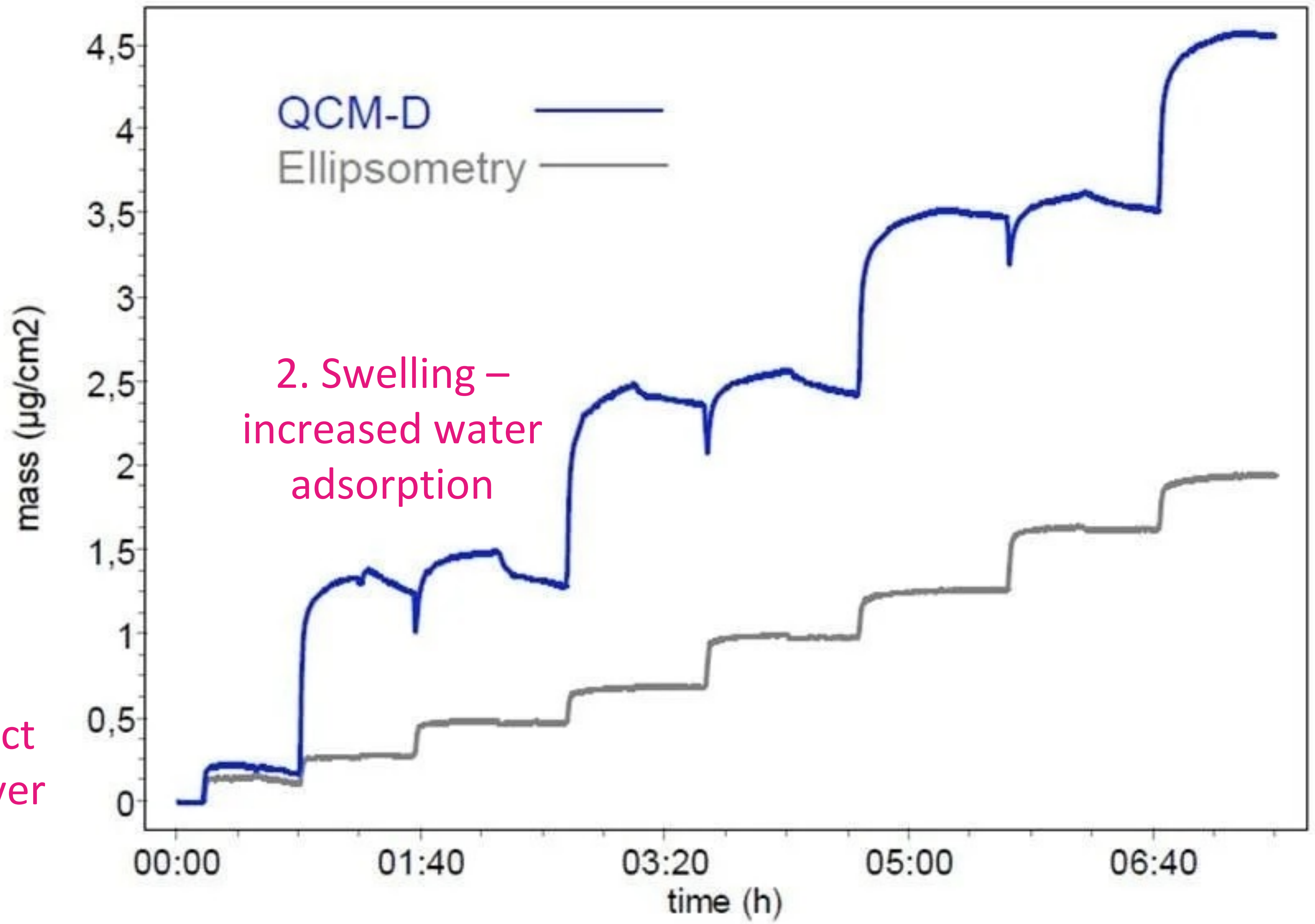


Polyelectrolyte multilayer

De Boer & Schroën | Sep. Purif. Tech.| 2024



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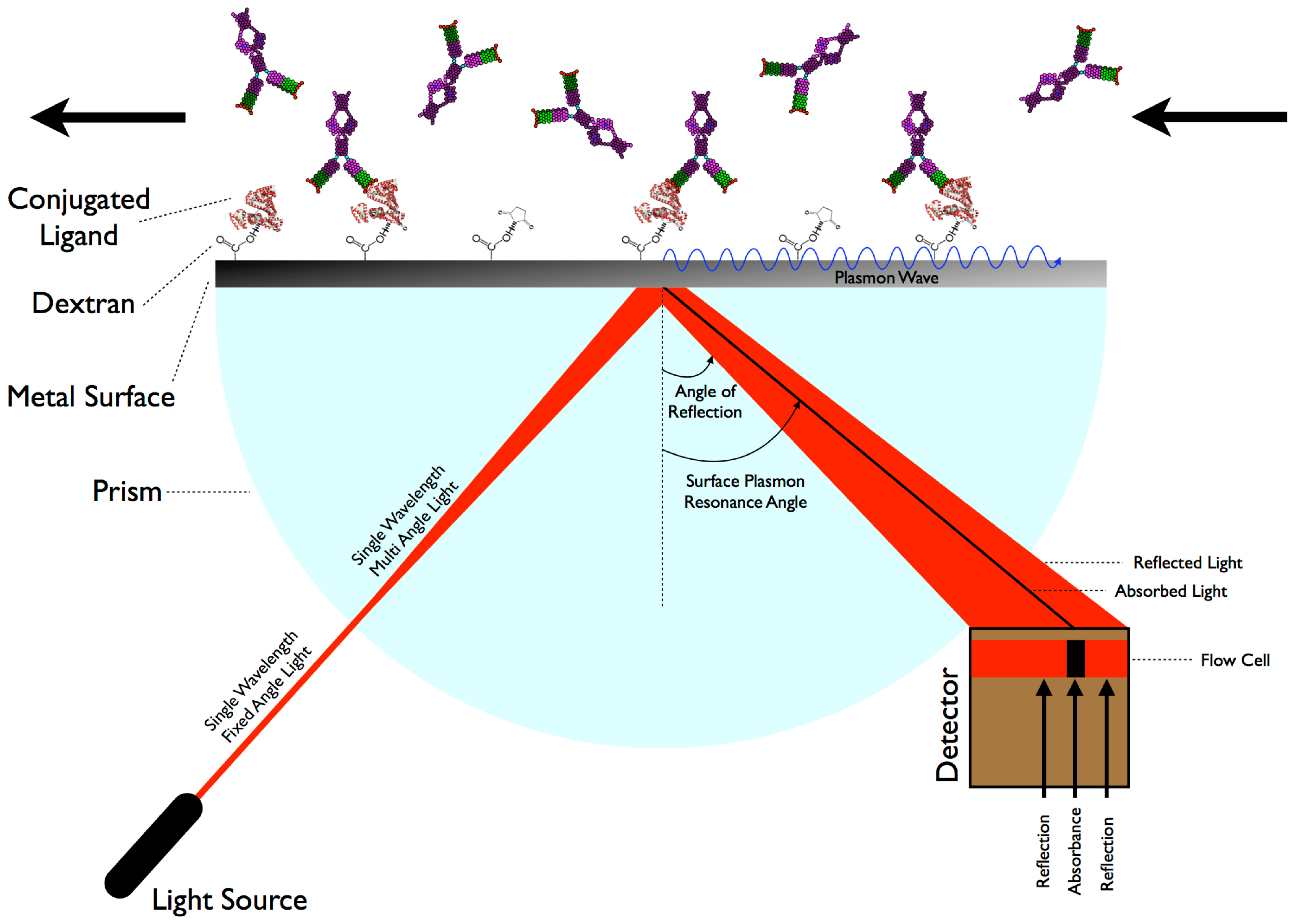
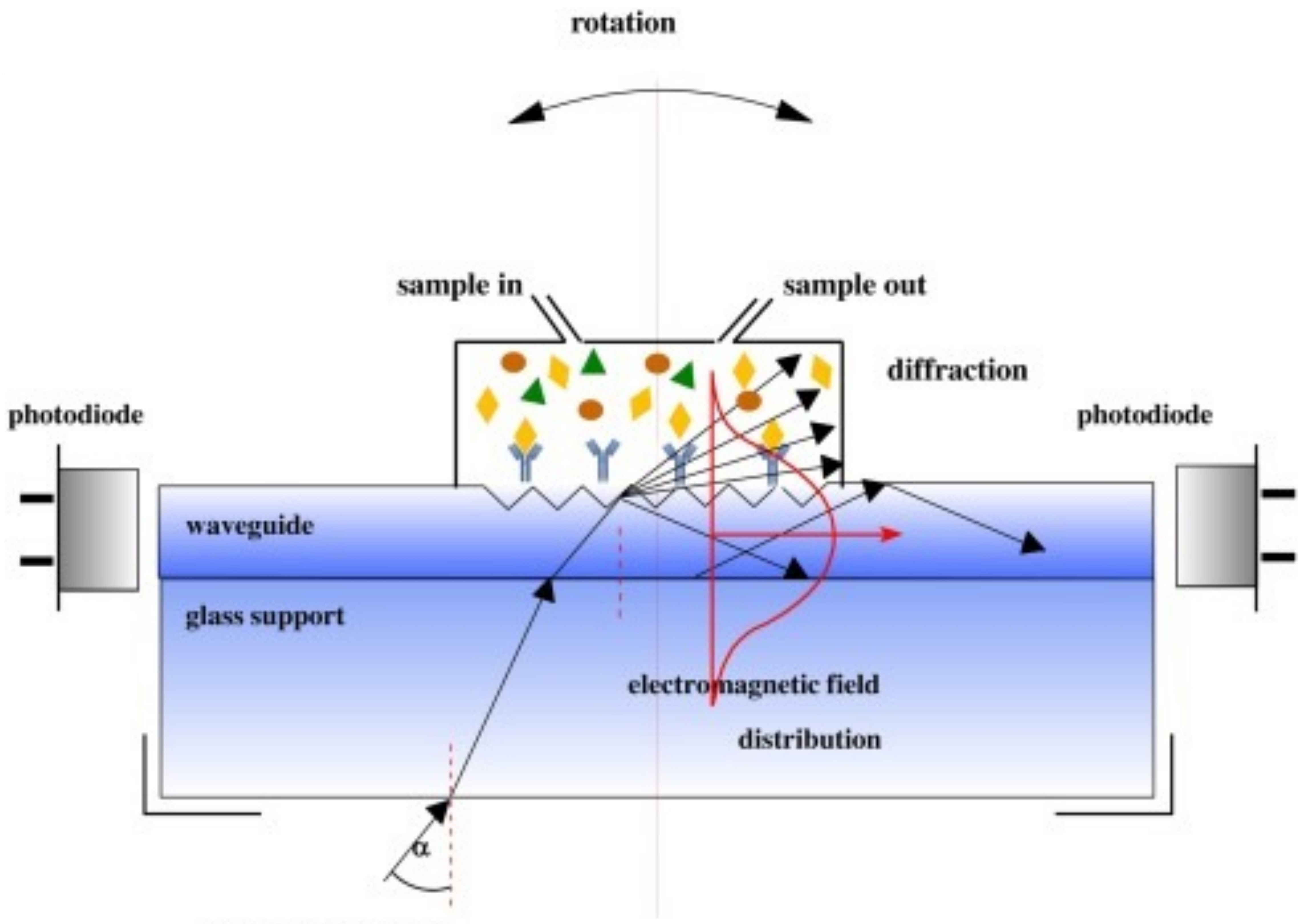
OWLS and SPR – Binding Kinetics and True Dry Mass Changes

OWLS: Optical waveguide light-assisted spectroscopy

SPR: Surface plasmon resonance spectroscopy

Measure changes in **refractive index** near a surface as molecules bind





Adanyi *et al.* | *Sens. Actuators B* | 2017

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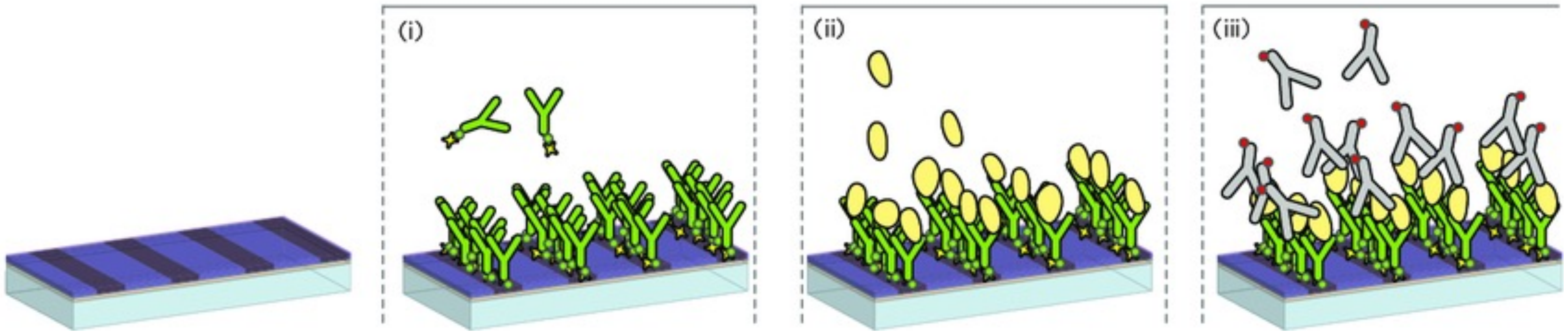
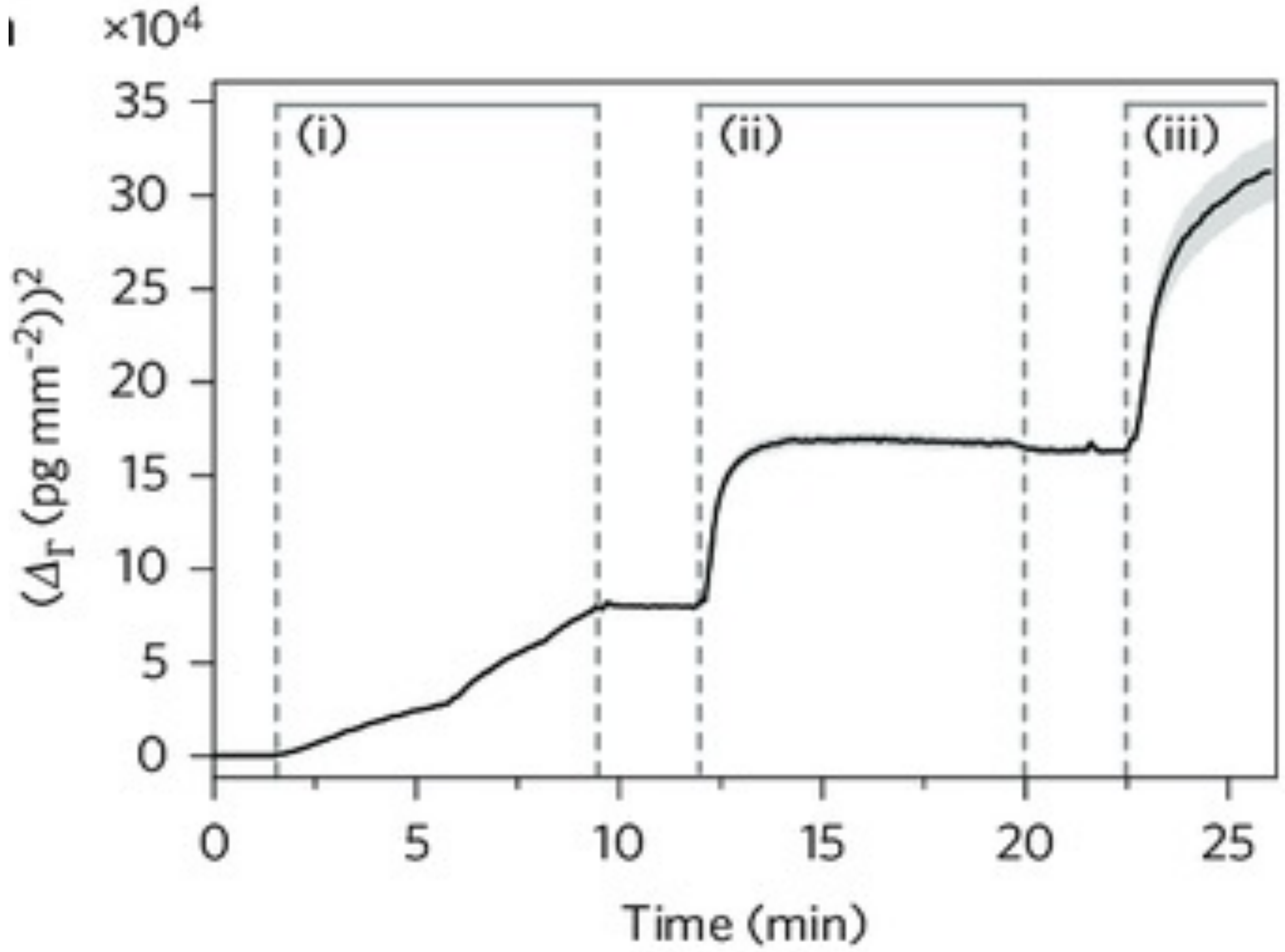
OWLS and SPR – Binding Kinetics and True Dry Mass Changes





Gatterdam *et al.* | *Nat. Nanotechnol.* | 2017

OWLS *vs.* SPR – Binding Kinetics and True Dry Mass Changes

Feature	SPR	OWLS
Optical mode	Surface plasmons on gold	Guided modes in a waveguide
Sensing depth	~200 nm	~150–200 nm
Substrate	Gold	SiO_2/TiO_2-based waveguides
Sensitivity	0.1 ng/cm^2	1 ng/cm^2
Strength	Kinetic measurements (fast interactions)	Quantitative surface mass density (pg/mm^2)
Weakness	Susceptible to environmental changes (temperature, buffer changes)	Susceptible to environmental changes (temperature, buffer changes)

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Key Takeaways

- We recapped the basic principles of light propagation through materials
- For ellipsometry, optical properties and layer thickness are determined
- Ellipsometry can be combined with QCM-D for both dry and wet mass
- Real-time monitoring of dry mass changes can be conducted by SPR/OWLS
- Choosing the technique is often dependent on the system you are probing

Summary of Today's Class

We expanded our toolbox of surface characterization techniques:

- ➢ Atomic force microscopy/Fluid force microscopy
- ➢ Quartz crystal microbalance with dissipation monitoring
- ➢ Ellipsometry
- ➢ Surface plasmon resonance and optical waveguide lightmode spectroscopy

Different surface properties (viscoelasticity, mechanical, thickness) can be explored using a combination of these techniques at interfaces

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