ENVIRONMENTAL STUDIES AND LIFE SCIENCES

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Mechanobiology

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- Most cellular functions depend on the mechanical properties of both the environment and the cell itself.
- Mechanobiology studies how cells sense and respond to physical cues and forces and how they transduce mechanical signals into biochemical responses.
- Mechanobiology has emerged as a new and growing field that attracts researchers from disciplines ranging from cell and developmental biology, to bioengineering, material science and biophysics.
- Technical advances have recently made possible the study of intracellular mechanotransduction, i.e. how forces are transmitted within the cell at the subcellular level.
- Applying and measuring forces inside cells allows to address key questions.
- These processes involve the deformation and rearrangement of cellular components, which can be studied by either applying or monitoring forces in real-time.

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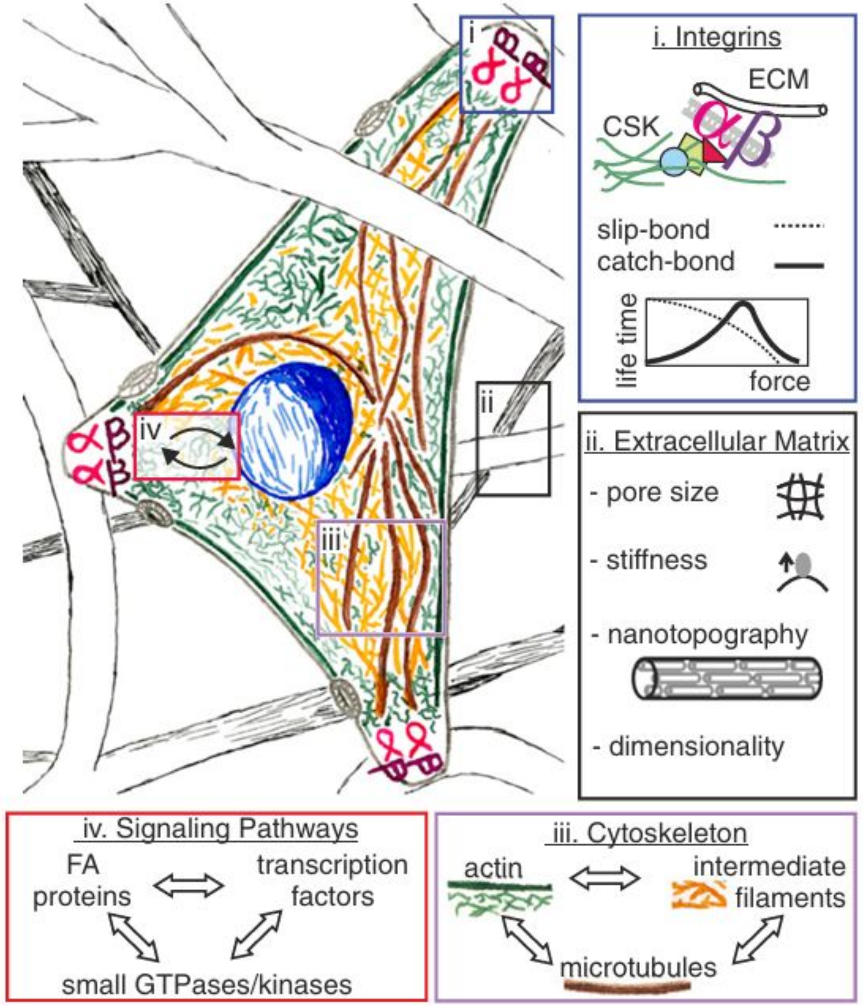

(i) Integrins are composed of an α (pink) and β subunit (purple) and are clustered in focal adhesions (FAs) together with other FA proteins (triangle, square and circle). Adhesions connect the extracellular matrix (ECM) and the (actin) cytoskeleton (CSK). Integrins can be classified as slip-or catch bond adhesion molecules, which differ in their bond lifetime under an applied force.
(ii) ECM provides multiple cues to the cell, specifically pore size, stiffness, nanotopography and dimensionality.
(iii) CSK is composed of actin (green), intermediate filaments (yellow) and microtubules (brown).
(iv) Summary of signaling pathways.

Schematic showing a cell inside a three dimensional fibrous extracellular network.

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- Six different state-of-the-art experimental techniques that are specially adapted to the study of the mechanical properties of sub-cellular components are highlighted.
- They are (ordered from force generators to mechanical sensors): optogenetics, bacterial cells and nanorobots, optical tweezers (OT), Brillouin microscopy, tension probes, and magnetic particles.
- These techniques allow for a higher degree of precision in space and time, and can thus provide information about the organelle of interest without simultaneously altering other cell components.

Table 1 | Physical quantities and orders of magnitude

Technique	Description	Order of magnitude and unit
Optogenetics	Force of individual myosin motor[a]	pN
Bacterial cells/ nanorobots	Force of bacterial cell upon collision	unknown
Optical tweezers	Force exerted by optical trap	pN to nN
Brillouin microscopy	Elastic moduli	kPa to GPa
Tension probes	Tension	0.01 to 1 mN/m
Magnetic particles	Force acting on particles	fN to nN

G giga 10^9, *n* nano 10^{-9}, *p* pico 10^{-12}, *f* femto 10^{-15}.

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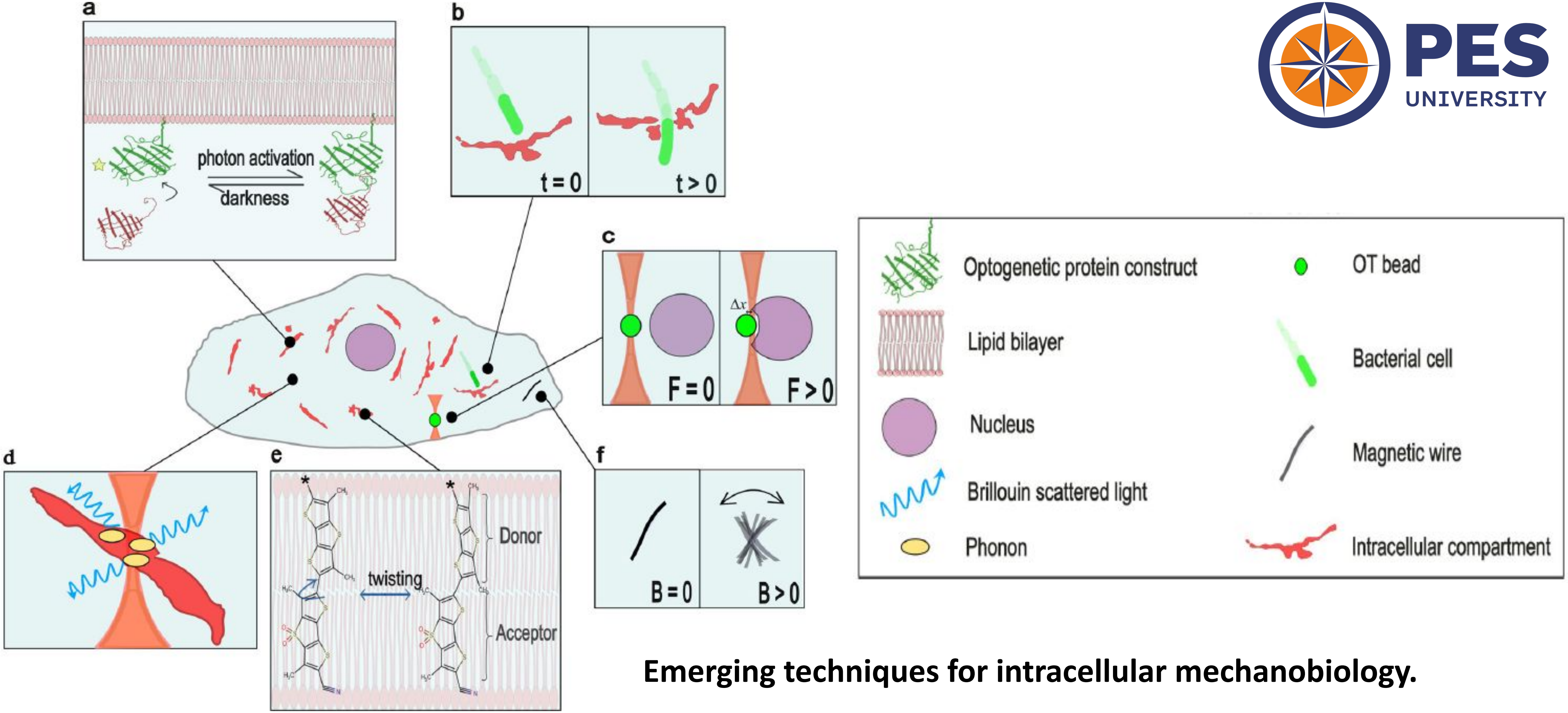

Emerging techniques for intracellular mechanobiology.

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a. Optogenetics - An anchor protein (green) is inserted into the membrane of a specific organelle. Blue light activation from a laser causes recruitment of genetically modified target protein, often a molecular motor, to the anchor. The yellow star indicates conformational change of the anchor protein upon photoactivation.

b. Bacterial cells and nanorobots - A single bacterial cell (green) moves in an uncontrolled manner through cytoplasm, propelled by its actin comet tail. Collisions with intracellular organelles generate intracellular forces. For instance, collision with mitochondria causes mitochondrial fission.

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Mechanobiology

c. Optical tweezers - A µm-diameter bead (green) trapped by optical tweezers (OT) can push against and deform the nucleus (purple). The infra-red (IR) laser generating optical trap can be moved to displace the bead within the cytoplasm or, if the position of the trap is fixed, nucleus can be moved towards the bead.

d. Brillouin microscopy - Photons from the laser interact with phonons (yellow) in an intracellular structure and cause Brillouin scattering to occur. Interaction between light and phonons induces a shift in frequency of scattered light which can be related to the rheological moduli of intracellular compartments.

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e. Tension probes - Mechanical planarization of the twisted Flipper molecule increases conjugation and thus connects the donor and acceptor regions. This difference is at the origin of the difference in the lifetimes. The stars (*) refer to different functional groups, which target specific organelle membranes.

f. Magnetic particles - In Magnetic Rotational Spectroscopy (MRS), magnetic rods of a few micrometres in length will oscillate back and forth in the cell cytoplasm under a rotating magnetic field or switch to a rotating regime depending on the frequency of the rotating field. Magnetic field is generated by an electromagnet positioned near the sample.

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THANK YOU

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