

A developmental biologist's guide to mechanics

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ABSTRACT

Developmental biology seeks to explain how living systems self-organize into functional, robust forms. While molecular and genetic approaches have revealed how biological information is encoded and processed, they often do not explain how this information is translated into physical shape. Here, we introduce the mechanical principles underlying tissue morphogenesis, aimed at developmental biologists with little background in physics. This Primer is structured around three core pillars. First, force generation describes how active and passive processes within cells and tissues drive deformation and motion. Second, constitutive behavior defines how living matter responds to these forces, spanning elastic, viscous and plastic regimes. Third, geometry and boundary constraints set the spatial constraints that shape mechanical interactions at the tissue and organismal levels. Together, these elements provide a framework for understanding how form emerges from the interplay between forces, material properties and geometry. We illustrate key examples across developmental processes and highlight recent advances and future challenges, integrating mechanical and molecular perspectives to guide the study of morphogenesis.

KEY WORDS: Physics of morphogenesis, Force generation, Constitutive behavior, Boundary constraints, Shapes

Introduction

Development is the process by which living matter organizes itself into a functional organism. Across biological systems, this transformation is remarkably robust: tissues reproducibly acquire precise shapes, organs emerge at well-defined locations, and coordinated dynamics unfold despite biological noise and environmental variability. Explaining the mechanisms that coordinate the cellular ballet that shapes complex multicellular organisms is one of the central challenges of life sciences. Historically, the study of embryogenesis was framed through the opposing theories of preformation and epigenesis (Van Speybroeck et al., 2002; Fagan and Maienschein, 2022). Preformation posits that the organism exists in a fully specified, miniature form from the outset, with development amounting to its mere unfolding. In contrast, epigenesis proposes that organization emerges progressively through interactions within initially unstructured living material (Maienschein, 2014). With the progress of experimental embryology in the 19th century, epigenesis became the dominant conceptual framework (Tickle et al., 2023). However, it did not, on its own, provide a mechanistic account of how

the embryo organizes, and the focus consequently shifted toward identifying the processes that regulate and coordinate growth, motion and fate specification of embryonic matter.

Over the past decades, this effort has been largely driven by molecular and genetic approaches, which have uncovered how signaling pathways and regulatory networks control cellular behaviors across animals and plants (Tickle et al., 2023). These advances have profoundly reshaped our understanding of development. Nevertheless, they primarily address how biochemical information is encoded and processed, without addressing the question of how this information is translated into physical form (Keller, 2002). Morphogenesis inherently involves the movement and deformation of matter: cells divide, migrate, change shape and exert forces on one another, while tissues undergo large-scale deformations such as folding (Sawyer et al., 2010), elongation (Keller, 2006) and flow (Saadaoui et al., 2020). Consequently, these dynamic mechanical transformations remain difficult to evaluate or quantify using genetic approaches alone.

In the physical sciences, mechanics is precisely concerned with how forces generate motion and deformation of materials, and how these effects depend on material properties and spatial constraints. Across systems and scales, from soap bubbles minimizing surface energy to galaxies structured by gravitational interactions, mechanics provides a unifying framework to understand how form emerges from the interplay between forces, matter and geometry. Mechanics provides a natural and increasingly indispensable framework for developmental biology, particularly for growth and morphogenesis (Lecuit et al., 2011; Heisenberg and Bellaïche, 2013). It offers a way to connect local cellular behaviors to large-scale tissue deformations and to formulate quantitative, predictive descriptions of how biological organization and form emerge. The idea that physical forces contribute to biological organization has deep roots – from early attempts to explain embryonic organization through physical attraction between future adjacent body parts (Moreau de Maupertuis, 1745) to D'Arcy Thompson's seminal arguments on growth and form (Thompson, 1917). This concept has gained renewed relevance with modern experimental tools, enabling predictive models in which biological organization and form emerge from well-defined sets of interactions across biological scales.

In this Primer, we propose that the mechanical framework for describing developmental processes can be organized around three fundamental pillars. First, one must identify the forces that act on the system. Akin to gravitational forces shaping solar systems, biophysical forces shape the living matter. These forces include active cellular processes, such as growth, migration, contractility and adhesion, as well as passive processes resulting from cellular or tissue deformations. Together, these forces provide the inputs that shape tissue dynamics. Second, one needs to characterize the constitutive behavior of living matter, which determines how forces are transformed into deformations. Cells and tissues exhibit complex mechanical responses, often combining elasticity, viscosity and plasticity (see Glossary), and can actively remodel

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Glossary

Boundary constraints

Physical or mechanical constraints at the edges of a biological system that determine how it behaves. For example, whether a cell/tissue is attached to a substrate (e.g. tissue–tissue boundaries), confined by neighboring cells (e.g. cell–ECM contacts) or free to move (e.g. epithelial surfaces).

Buckling

Mechanical instability in which a structure under compressive stress undergoes a transition from a straight or flat configuration to a bent, wrinkled or folded shape to relieve the stress.

Continuum mechanics

A framework that treats materials as continuous media, ignoring their discrete cellular/molecular structure, to model how they deform at scales much larger than their cellular/molecular structure.

Creep

The slow, continuous deformation of a material under constant stress (e.g. a cell sheet gradually stretching when pulled by steady forces).

Elasticity

The ability of a material to return to its original shape after deformation.

Enthalpic elasticity

Elasticity arising from energy changes in molecular bonds or interactions (e.g. stretching covalent bonds or hydrogen bonds).

Friction

The resistance to motion between surfaces in contact.

Entropic elasticity

Elasticity driven by a reduction in conformational entropy (e.g. stretching a disordered polymer reduces its randomness, generating a restoring force).

Mechanical energy

The energy associated with motion or deformation. In biological tissues, it is stored primarily as elastic energy in deformed structures and can be released to generate restoring forces or dissipated during deformation.

Persistence length

The characteristic length scale over which a polymer or filament remains straight before thermal fluctuations cause it to bend.

Plasticity

Irreversible deformation phenomenon that occurs above a stress threshold.

Poroelectricity

Time-dependent mechanical behavior arising from the coupling between deformation of a porous solid matrix and fluid flow through its pores.

Pressure

A type of stress that acts equally in all directions (e.g. turgor pressure in plant cells). Unit: pascal (Pa).

Rheology

A branch of physics that studies the deformation and flow of matter to provide a foundational understanding of material behavior.

Strain

A dimensionless measure of deformation that quantifies how much a material stretches, compresses, or shears relative to its original shape.

Stress

Force per unit area within a material. Stress can be normal (stretching or compression) or tangential (shear). Unit: pascal (Pa).

Tension

A restoring force that resists expansion; its units scale with the dimensionality of the structure: 1D (measured in Newtons, N), 2D (measured in Newtons per meter, N/m – see surface tension), or 3D (measured in Newtons per square meter, N/m²).

Surface tension

A restoring force that reflects how strongly a surface resists expansion. It is also defined as the energy required to increase the surface or interface of a material by one unit area. Unit: J·m⁻² or N/m.

Viscoelasticity

Mechanical behavior combining elastic energy storage and viscous dissipation, causing the response to depend on time.

Viscosity

A fluid's resistance to flow; in a tissue, it reflects how rapidly cells can rearrange to dissipate mechanical stress and change tissue shape.

their internal structure, thereby altering their effective mechanical properties. Understanding how tissues dynamically deform in response to forces therefore requires appropriate measurements and models. Third, geometry and **boundary constraints** define the spatial canvas on which forces act. Tissue architecture, their boundaries and their microenvironments set the constraints under which mechanical interactions unfold. Geometry not only shapes these interactions but also feeds back on them as mechanically active domains progressively deform (Hannezo and Heisenberg, 2019).

Together, these three interdependent elements – force, constitutive behavior and geometry – define a minimal and general framework for describing the mechanics of morphogenesis. In this Primer, we examine how each contributes to developmental processes and how their interplay drives the emergence of biological form, providing three complementary layers for constructing mechanical models of morphogenesis.

Pillar I – Forces in biological systems

Morphogenesis – the generation of biological form – is the process by which cells and tissues are transformed into functional organs and organisms. This immediately raises a fundamental question: where do the forces that shape developing tissues come from? Although these forces originate from molecular processes, they are integrated across cells and tissues to generate the large-scale deformations that drive morphogenesis. Describing this collective behavior does not require tracking every molecular interaction individually. Instead, their combined effects can be represented by effective tissue forces, the balance of which governs tissue motion.

Generation of forces during development

Forces in living tissues can be classified as either active, generated by the conversion of chemical energy into mechanical work, or passive, arising from the deformation of cells and tissues.

Active forces

Active mechanical forces arise from the conversion of chemical energy into mechanical work. Although generated through diverse mechanisms, they all rely on continuous energy input to produce forces that deform cells locally and generate tissue-scale stresses (Table 1).

ATP-dependent molecular motors are a major source of active forces during morphogenesis. Myosins, kinesins and dyneins convert ATP hydrolysis into mechanical work (Vale, 2003). Among these, myosin II is the primary generator of contractile forces during morphogenesis (Howard, 2001; Murrell et al., 2015). Myosin proteins assemble into bipolar mini-filaments that pull actin filaments together, driving actomyosin network contraction (Bendix et al., 2008; Lenz et al., 2012). This generates tension, enabling cells to remodel their shape and interactions with neighboring cells and the extracellular matrix (ECM) (Kasza and Zallen, 2011; Martin et al., 2009; Munjal and Lecuit, 2014).

Active forces also emerge from cytoskeletal polymerization. Actin polymerization at the cell periphery pushes the plasma membrane outward, promoting protrusion formation and migration (Miyata et al., 1999; Mogilner and Oster, 2003; Pollard and Borisy, 2003). Microtubule polymerization similarly generates pushing forces involved in spindle assembly, nuclear positioning and cell polarity. Unlike molecular motors, which mainly generate pulling forces, polymerization-driven mechanisms produce protrusive forces through filament growth (Antunes et al., 2013; Gorfinkel, 2016; Miao and Blankenship, 2020) (Fig. 1).

Table 1. Major sources of mechanical forces in developing tissues

Force category	Example	Scale	Physical description	Typical magnitude	Measurement methods	Key references
Molecular motor forces	Myosin motors	Molecular	ATP-driven force generation	~1-5 pN	Optical tweezers	Finer et al., 1994
Protrusive forces	Actin polymerization	Subcellular	Polymerization-driven pushing	~1-10 pN	Optical tweezers	Footer et al., 2007; Marcy et al., 2004
Cell surface tension	Cortex/membrane tension	Subcellular/cellular	Effective surface tension	~0.1-1 nN/ μ m	AFM, micropipette aspiration	Chugh et al., 2017; Guevorkian et al., 2010
Cell–cell interfacial tension	Adherens junctions	Subcellular/cellular	Effective surface tension	~0.1-1 nN/ μ m	Laser ablation, micropipette aspiration, optical tweezers	Bambardekar et al., 2015; Liang et al., 2016; Maître et al., 2012; Rauzi et al., 2008
Pressure	Osmotic/lumen pressure	Cellular	Isotropic stress (pressure)	~10-1000 Pa	Micropipette, micropressure probe	Chan et al., 2019; Dumortier et al., 2019
Traction forces	Cell–substrate adhesion	Cellular	Force transmitted to ECM	~1-100 nN per cell	Traction force microscopy	Dembo and Wang, 1999; Maskarinec et al., 2009; Tan et al., 2003
Turgor pressure	Plant cell osmotic pressure	Cellular	Internal hydrostatic pressure generated by osmotic water influx	~0.1-1 MPa	AFM indentation	Beauzamy et al., 2015
Tissue-scale stress	Collective tissue mechanics	Tissue	Continuous stress field	~10-1000 Pa	MSM, uniaxial tensile testing, oil droplet	Campàs et al., 2014; Wiebe and Brodland, 2005; Tambe et al., 2011

Mechanical quantities are reported as forces (pN), tensions (N/m) or stresses (Pa), depending on the scale and measurement method (Roca-Cusachs et al., 2017; Sugimura et al., 2016; Villeneuve et al., 2025).

AFM, atomic force microscopy; ECM, extracellular matrix; MSM, monolayer stress microscopy.

Cells can also generate forces through fluid transport. ATP-dependent ion pumps establish osmotic gradients across membranes, driving water influx through aquaporins (Hoffmann et al., 2009; Verkman, 2009) (Fig. 1A). Water accumulation in lumens or confined spaces generates hydrostatic pressure that deforms surrounding tissues (Chan et al., 2019; Navis and Bagnat, 2015; Chugh et al., 2022; Dumortier et al., 2019). Compared with cytoskeletal forces, osmotic pressures can reach larger magnitudes, enabling deformation over greater spatial scales (Table 1).

The consequences of pressure-driven forces vary across biological systems. In animals, pressure gradients contribute to lumen formation, tissue deformation and fluid-mediated morphogenesis. Along similar lines, in plants, osmotic water uptake generates turgor pressure against the cell wall; consequently, local cell wall relaxation allows this pressure to drive irreversible cell expansion and growth (Cosgrove, 2005).

Together, these mechanisms generate contraction, protrusion and pressure-driven expansion that collectively shape tissues during morphogenesis in both plants and animals.

Passive forces

When cytoskeletal filaments, membranes and other cellular structures are stretched, compressed or sheared, they store mechanical energy and generate restoring forces through their intrinsic mechanical properties, including polymer elasticity, membrane tension and intermolecular interactions (Bray, 2001). A classic example is the elastic protein titin in animal skeletal muscle, which resists overstretching and recoils like a rubber band (Granzier and Labeit, 2004). Likewise, intermediate filaments do not generate active forces but contribute to passive mechanics by organizing, transmitting and resisting forces within the cytoskeleton, thereby maintaining mechanical integrity during morphogenesis. In addition

to these elastic restoring forces, mechanical energy is dissipated through viscous processes arising from internal friction during deformation. Unlike active forces, these passive mechanical responses require no energy input during force generation and instead reflect the material properties of biological structures and their tendency to relax toward lower-energy configurations (see Pillar II).

From forces to stress across scales

Mechanical forces in developing systems are generated and transmitted across multiple spatial scales, from individual molecules to whole organisms. At each scale, the origin of these forces, their measurement and their characteristic magnitudes differ (Table 1). Although generated locally, forces are transmitted and integrated across cells and tissues to drive coordinated morphogenesis.

Within cells, forces generated by molecular motors and cytoskeletal polymerization are transmitted through interconnected cytoskeletal networks – including actin filaments, microtubules and intermediate filaments – as well as through adhesion complexes linking the cytoskeleton to neighboring cells and the ECM (Parsons et al., 2010; Paul et al., 2008). This mechanical coupling enables forces to propagate beyond their sites of origin. For example, the pushing active force generated by actin polymerization at the cell periphery is transmitted through the cytoskeletal network, allowing localized polymerization to drive directional protrusion and cell migration even in regions distant from the polymerizing filaments themselves (Miyata et al., 1999; Mogilner and Oster, 2003; Pollard and Borisy, 2003).

At the subcellular scale, forces are distributed across structures such as the cell cortex, plasma membrane, cell–cell junctions and cytoskeletal networks, rather than acting at discrete points (Zuidema et al., 2020; Gardel et al., 2010). They are therefore best described as

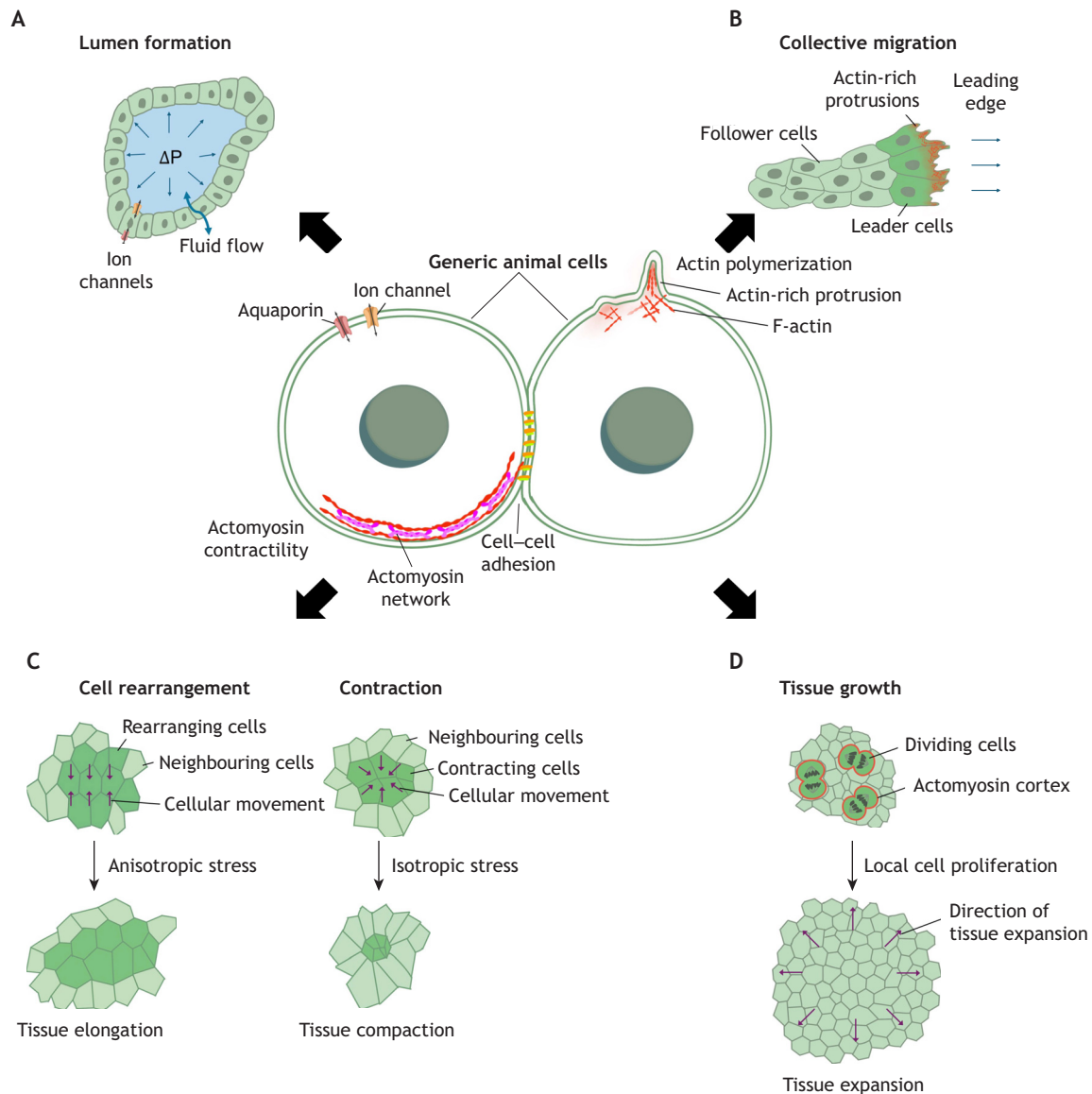


Fig. 1. Intracellular force-generating mechanisms drive tissue-scale mechanical behaviors. The central schematic provides an overview of the major cellular force-generating mechanisms in developing tissues and serves as the basis for the four surrounding panels, which illustrate how these mechanisms generate distinct tissue-scale mechanical behaviors. It includes actomyosin contractility, actin polymerization, cell–cell adhesion and ion transport through membrane channels. These processes generate and transmit forces within and between cells. (A) ATP-dependent ion transport establishes an osmotic pressure difference (ΔP), driving water influx into the lumen. Black radial arrows indicate the outward mechanical effect of the luminal pressure during lumen expansion. (B) Actin polymerization at the tissue edge generates protrusive forces that drive coordinated, directional collective cell migration. Here, leading edge refers to the advancing front of a moving cell group, featuring specialized leader cells, membrane protrusions and active environmental sensing. (C) At the tissue scale, anisotropic stress drives cell rearrangement and tissue elongation. Isotropic stress at the tissue scale leads to uniform contraction without directional deformation. (D) Tissue growth arises from local cell proliferation, leading to an overall increase in tissue size.

mechanical **tension** – the distributed restoring force that develops in response to deformation. In cells, tension arises both actively through molecular motors and passively from the elastic resistance of membranes, cytoskeletal polymers and adhesive structures.

At the cellular scale, forces generated at different subcellular locations are integrated through mechanical coupling (Murrell et al., 2015). During cell migration, for example, protrusive forces at the leading edge are coordinated with myosin II-dependent contractility at the rear and transmitted to the ECM through substrate adhesions (Fig. 1B). This mechanical integration enables coordinated cell behaviors, including shape changes and force transmission to neighboring cells and the ECM (Gardel et al., 2010).

When multiple cells are mechanically coupled, forces are transmitted across tissues through continuous mechanical networks spanning neighboring cells and their extracellular environment, both in animal (Charras and Yap, 2018) and plant (Coen and Cosgrove, 2023) tissues. As these forces integrate across many cells, their collective effect drives tissue-scale mechanical behavior. At the tissue scale, mechanical behavior is often described in terms of stress (defined as force per unit area), which captures how forces are distributed within a tissue and their contribution to large-scale deformation.

Stress is classified by the direction of force application. Normal stress acts perpendicular to a surface and may be tensile (that results

in stretching) or compressive (leads to compression). Shear stress arises from tangential forces and tends to distort cell or tissue shape without necessarily changing their volume. The spatial distribution of stress also influences tissue deformation. Anisotropic stress, which differs with direction, promotes cell rearrangements and tissue elongation, whereas isotropic stress, acting equally in all directions, favors uniform contraction (Fig. 1C).

In addition to stress-driven deformation, tissue shape can also change through growth arising from local increases in tissue mass. While stress-driven processes redistribute existing material, growth expands tissue size by adding new material. In the absence of external constraints, tissues generally expand uniformly (Fig. 1D). However, when growth is spatially heterogeneous or mechanically constrained by the surrounding environment, incompatible deformations generate internal stresses (see Pillar III) (Ambrosi et al., 2011).

Force balance governs deformation and motion

In many embryonic and developing tissues, the low mass of cellular structures and strong dissipative properties of biological materials make inertial forces negligible compared with active and passive forces. Thus, tissues can be approximated as being in quasi-static mechanical equilibrium, where stresses are balanced at each instant. However, inertia may become important in faster physiological processes or those involving fluid motion, such as blood flow (Fung, 1996).

Importantly, force balance in biological tissues does not imply the absence of motion. Tissue deformation and flow are driven by stress gradients, which arise from spatial variations in force generation, force transmission or material properties (see Pillar III). These gradients are opposed by dissipative processes, including friction and mechanical resistance from neighboring cells or the environment, such that tissue motion emerges from the balance between driving forces and resistance (Mayer et al., 2010). Accordingly, local differences in force generation or transmission can drive coordinated tissue movements, as illustrated by tissue-scale cell flows during zebrafish gastrulation and polarized cell intercalation during *Drosophila* germband extension (Behrndt et al., 2012; Bertet et al., 2004).

Because tissues are dissipative, mechanical energy is continuously lost through processes such as cytoskeletal remodeling and cellular rearrangements. Sustained tissue motion, therefore, requires continuous force generation to compensate for these losses. Friction and mechanical resistance further regulate how stress gradients are converted into tissue motion, as discussed in the next section.

Pillar II – Constitutive behavior: how tissues respond to forces

After considering the forces that act during morphogenesis, the next question is how embryonic tissues deform in response to them. In continuum mechanics, this relation is described by a constitutive law, which links stress to strain, defined as the deformation of the material. In developmental systems, the relation between stress and strain is a central determinant of morphogenesis: the same force can produce a reversible deformation or a permanent change in shape, depending on whether a tissue responds predominantly as an elastic solid, a viscous fluid, a viscoelastic material or a plastic body. Morphogenesis therefore depends not only on where and when forces are generated, but also on how tissues store, dissipate or irreversibly convert mechanical inputs into changes in shape (Clément et al., 2017; Lenne and Trivedi, 2022).

Mechanical responses across time and force scales

The simplest constitutive behaviors of materials can be distinguished by observing deformation during loading (when a force is applied) and recovery after unloading (when the force is removed) (Fig. 2A). An elastic material (Fig. 2Aii), such as a rubber band, stores mechanical energy and recovers its initial shape after the force is removed. A viscous material (Fig. 2Ai), such as honey, progressively flows and retains the resulting deformation. A plastic material (Fig. 2Aiii), on the other hand, undergoes an irreversible structural change after the applied stress exceeds a yield threshold; for example, a paper clip remains bent after being deformed beyond its elastic limit. Most tissues combine these responses and are therefore ‘visco-elasto-plastic’ (Schötz et al., 2013; Forgacs et al., 1998).

Simple rheological models describe these combinations using springs and dashpots, which represent elastic storage (solid behavior) and viscous flow (liquid behavior), respectively. In the Maxwell model (Fig. 2Aiii), a spring and a dashpot are connected in series. The material initially deforms elastically like a spring, but then it continues to flow like a liquid under sustained stress. When the applied force is removed, the elastic deformation recovers (as the spring part bounces back), whereas the viscous deformation remains. This model therefore represents materials that transiently store stress but relax through long-term flow, such as living tissue changing shape through cellular rearrangements. In the Kelvin–Voigt model (Fig. 2Aiv), the spring and the dashpot are connected in parallel: the viscous component delays deformation, whereas the elastic component (the spring) limits it to a finite value. The material consequently deforms progressively under sustained stress and gradually recovers after unloading. This behavior can arise in polymer networks such as the ECM or the cytoskeleton, where fluid drag and internal friction generate a viscous contribution that increases with deformation rate. As a result, the same material can appear relatively stiff when probed rapidly but softer when probed over longer timescales (Elosegui-Artola et al., 2023; Chaudhuri et al., 2020).

These models should not be regarded as fixed identities of particular tissues. Rather, they identify the dominant response over a given experimental timescale and force application mechanisms. Living tissues commonly display several relaxation times, nonlinear responses (Fig. 2Av) and active changes in their properties that require more complex descriptions (Storm et al., 2005; von Dassow et al., 2010; Tajvidi Safa et al., 2024). To investigate constitutive behavior in a tissue, several methods exist to access different spatial scales, timescales and deformation amplitudes, and may therefore reveal different apparent material properties (Box 1).

Microscopic origins of tissue elasticity

At microscopic scales, tissue elasticity arises largely from networks of actin, intermediate filaments, microtubules and ECM fibers (Fig. 2B). Their response depends on filament flexibility, crosslinking, connectivity, architecture and pre-stress (Fletcher and Mullins, 2010; Storm et al., 2005). Persistence length describes filament flexibility: filaments with short persistence lengths bend readily, whereas those with long persistence lengths remain straighter.

Several mechanisms usually coexist to drive tissue elasticity (Fig. 2C). At rest, flexible and semiflexible filaments are not perfectly straight as thermal agitation continuously bends them into fluctuating conformations. When the network is stretched, these thermally driven bending fluctuations are progressively suppressed, reducing the number of conformations available to each filament. The tendency of the filaments to recover their fluctuating state

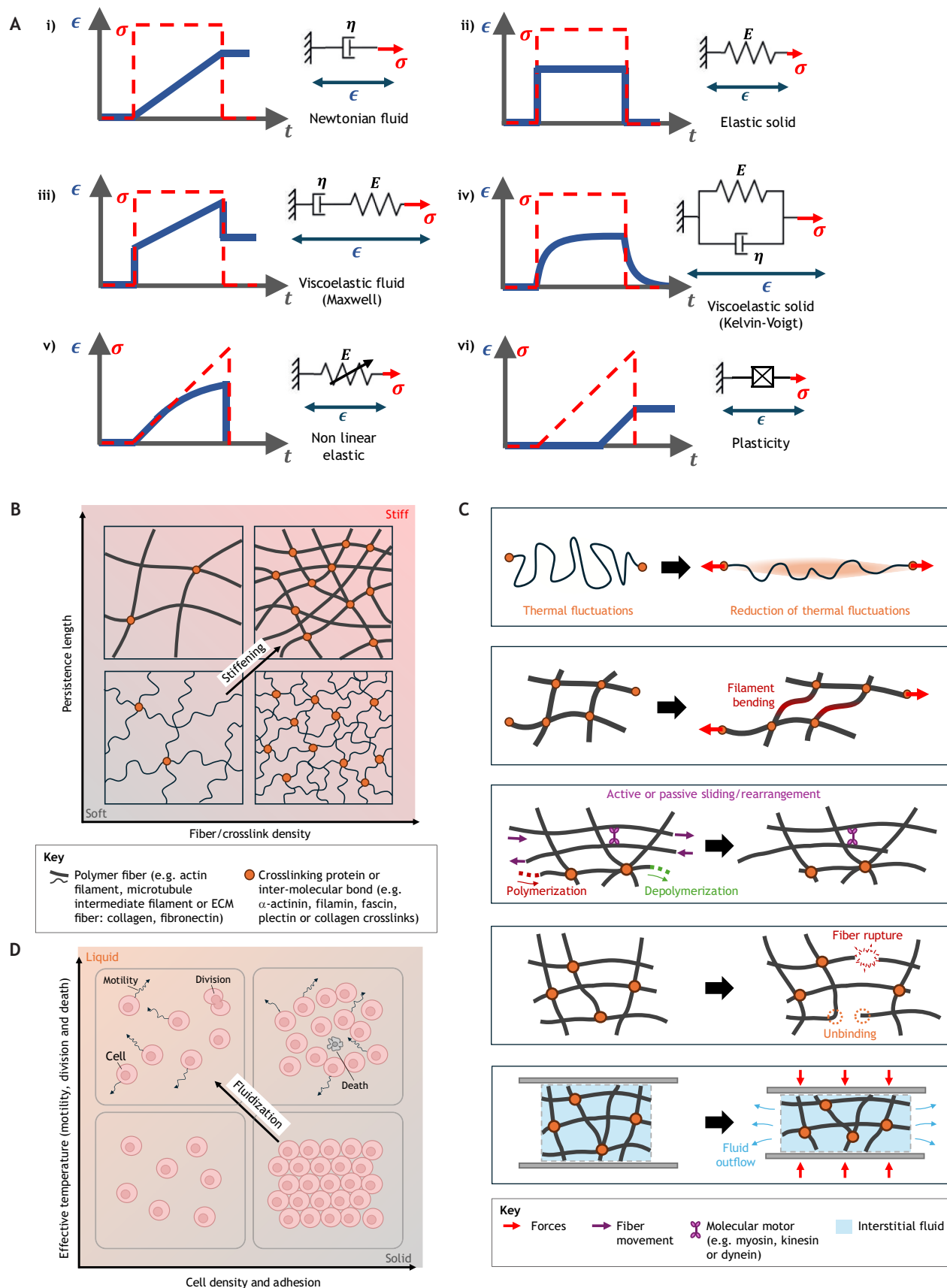


Fig. 2. See next page for legend.

Fig. 2. Microscopic and mesoscopic origins of tissue constitutive behavior.

(A) Minimal rheological models of constitutive behavior. The red dashed lines represent imposed stress, σ , and the blue lines the resulting strain, ϵ , over time. Springs of modulus (E) represent elastic energy storage, dashpots of viscosity (η) represent viscous dissipation, and yield elements represent irreversible deformation above a threshold stress. Different combinations reproduce Newtonian, elastic, Maxwell and Kelvin–Voigt responses, as well as nonlinear elasticity and plasticity. (B) Polymer-network architecture and stiffness. Schematic map showing how filament persistence length and fiber/cross-link density regulate network mechanics. Biological polymer networks include the actin, microtubule and intermediate-filament cytoskeletons, as well as extracellular matrix (ECM) networks containing collagen, fibronectin and laminins. Persistence length reflects filament resistance to bending. Sparse networks of flexible filaments respond mainly through **entropic elasticity**, whereas stiffer filaments and denser or more highly cross-linked networks favor enthalpic deformation through filament bending and stretching. Orange circles indicate cross-links, and the diagonal arrow indicates increasing stiffness. (C) Microscopic origins of time-dependent mechanics. Entropic elasticity results from the straightening of thermally fluctuating filaments, whereas **enthalpic elasticity** arises from filament bending or stretching. Filament polymerization, depolymerization, motor-driven or passive sliding, and network rearrangement promote fluidity and viscoelastic stress relaxation. Fiber rupture and cross-link unbinding enable irreversible remodeling and plastic deformation. In hydrated networks, compression-driven fluid redistribution generates poroelastic relaxation. (D) Mesoscopic regulation of tissue fluidity. Schematic phase diagram showing the balance between structural constraints and active fluctuations. Increasing cell density and adhesion restricts neighbor exchange and promotes a solid-like, jammed state. Increasing effective temperature, representing activity generated by cell motility, division, death and junctional fluctuations, promotes rearrangements and tissue fluidization.

generates an entropic restoring force. In parallel, deformation can directly bend and stretch filaments and molecular bonds, producing an enthalpic contribution. The balance between these forces depends on filament stiffness, network architecture, pre-stress and deformation amplitude (MacKintosh et al., 1995; Gardel et al., 2010; Broedersz and MacKintosh, 2014).

Fibrous materials such as collagen and fibrin often stiffen when stretched and respond differently to tension and compression (Han et al., 2018). Fiber alignment creates anisotropy, favoring force transmission, deformation or migration along particular directions (Wang et al., 2014, 2018). Furthermore, cells dynamically remodel the ECM through active synthesis, degradation, alignment and pre-stressing. Consequently, cells and the ECM form a coupled, active composite whose stiffness, anisotropy and relaxation properties evolve during development (Barriga et al., 2018; Walma and Yamada, 2020).

Dissipation, remodeling and fluid transport

The same biological networks that store elastic stresses also provide mechanisms for mechanical dissipation (Fig. 2C). Cytoskeletal and matrix networks are highly dynamic: filaments polymerize and depolymerize, crosslinkers bind and unbind, motors remodel network geometry, and fibers slide, rupture or reattach. A network may therefore appear to be elastic at short times but dissipate stress and appear to be fluid during longer perturbations (Lieleg et al., 2008; Broedersz et al., 2010; Mulla et al., 2019). Reversible molecular rearrangements generate viscoelastic relaxation without permanently changing network architecture. By contrast, bond rupture, persistent fiber reorganization, ECM degradation or matrix deposition remodel the material and can produce plastic changes (Walma and Yamada, 2020; Courbot and Elosegui-Artola, 2025).

Tissues also exhibit a distinct mechanism of relaxation because they are permeable materials saturated with interstitial fluid. As a tissue deforms, fluid flows relative to the cells and the ECM

Box 1. Methods to investigate mechanical properties of tissues

Whole-tissue deformation assay. Micropipette aspiration applies a controlled pressure and tracks tissue entry into a pipette. **Creep**, recovery or oscillatory protocols provide model-dependent estimates of elasticity, viscosity, relaxation times and interfacial tension, while microfluidic devices enable parallel measurements (Guevorkian et al., 2010; Landiech et al., 2024). Parallel-plate or unconfined compression similarly probes tissue viscoelasticity and interfacial tension, whereas confined or osmotic compression is sensitive to fluid redistribution and poroelasticity (Forgacs et al., 1998; Mgharbel et al., 2009; Dolega et al., 2021). Tensile tests measure stress–strain relationships, rate dependence and anisotropy in epithelial sheets and embryonic explants (Moore et al., 1995; Wiebe and Brodland, 2005). Bulk shear rheometry yields storage and loss moduli across frequencies, though it requires larger sample volumes.

Shape-relaxation assays. Aggregate fusion, rounding and spreading provide simple readouts of long-time flow. Incomplete or arrested coalescence can reveal elastic or yield-like behavior (Oriola et al., 2022).

Local indentation. AFM and micro- or nanoindentation map apparent stiffness, creep and stress relaxation from cellular to supracellular scales (Thompson et al., 2019; Viljoen et al., 2021). Interpretation depends on probe geometry, indentation depth, tissue thickness, adhesion, pre-stress and the contact model.

Passive and active micro-rheology. Passive tracking of embedded probes estimates local frequency-dependent viscoelasticity with little perturbation, although active fluctuations can complicate interpretation (Tseng et al., 2002; Wessel et al., 2015). Active optical or magnetic manipulation of beads and droplets provides local compliance, moduli and relaxation times (Bambardekar et al., 2015; Doubrovinski et al., 2017; Favre-Bulle and Scott, 2022).

Imaging-based elastography. Brillouin microscopy maps high-frequency longitudinal mechanical contrast, which is not directly equivalent to quasi-static Young's or shear moduli and depends on hydration and composition (Schlüßler et al., 2018; Prevedel et al., 2019). Optical coherence elastography maps internal displacement, strain or elastic-wave propagation in three dimensions (Larin and Sampson, 2017; Mason et al., 2023).

In all these approaches, constitutive parameters are inferred through analytical or computational models, rather than measured directly. Combining different loading rates, durations, amplitudes or probe sizes improves distinction between competing rheological mechanisms.

(Fig. 2C), coupling fluid transport to the elastic deformation of the solid scaffold (Biot, 1956). This response, called **poroelasticity**, produces time-dependent relaxation and is well established in soft tissue mechanics (Wang et al., 2020b) but its role in developmental morphogenesis remains comparatively underexplored.

Collective mechanical behavior of tissues

At the tissue scale, **rheology** also emerges from the collective organization of cells. A tissue can behave more fluid-like when cells rearrange by exchanging neighbors, allowing the tissue to flow (Dicko et al., 2017), and more solid-like when cells are mechanically constrained, or 'caged', by surrounding cells (Fig. 2D). This fluid-to-solid transition is often described in terms of jamming and unjamming (Mongera et al., 2018). In confluent tissues, such as epithelia, this transition is not controlled by density alone. Tissue fluidity is also regulated by multiple active processes, including cell shape, cell–cell adhesion, cortical tension, motility, cell divisions, apoptosis and junctional fluctuations. These active processes facilitate cell deformation, junctional remodeling and neighbor exchange, thereby helping cells overcome the mechanical barriers that constrain rearrangement (Ranft et al., 2010; Bi et al., 2016;

Lawson-Keister and Manning, 2021). Developmental systems provide clear examples of these principles. During vertebrate body-axis elongation, posterior tissues undergo a fluid-to-solid transition that spatially organizes tissue mechanics along the elongating axis (Serwane et al., 2017; Mongera et al., 2018). More generally, such collective transitions provide a framework for understanding how embryonic tissues switch between states that favor deformation, migration, sorting or stabilization (Petridou et al., 2021; Lenne and Trivedi, 2022; Hannezo and Heisenberg, 2022).

Mechanical properties as developmental signals

Tissue mechanical properties are not only determinants of deformation; they also provide signals that influence cell behavior. Cells sense the stiffness, viscoelasticity and architecture of their surroundings through adhesions, the cytoskeleton and the nucleus, converting mechanical cues into changes in signaling, gene expression, migration and cell fate. This process, known as mechanotransduction, creates feedback between tissue organization and mechanics: cells establish tissue properties, but these properties can in turn regulate developmental decisions (Engler et al., 2006; Janmey and Miller, 2011; Barriga et al., 2018; Walma and Yamada, 2020).

Pillar III – Dimensionality, boundary constraints and spatial heterogeneities

Mechanical models and descriptions of developmental processes are not defined by mechanical forces and material properties alone: they are also specified by the spatial and geometric frameworks in which these quantities exist. During development, geometry enters at multiple, tightly coupled levels: the shape and dimensionality of the system, the boundary constraints, and the spatial distribution of both force generation and material properties. These parameters determine how stresses are distributed, how deformations propagate, and ultimately which morphogenetic outcomes are accessible to a given system.

Dimensionality and shape

At the most basic level, the dimensionality and initial shape of a system set global constraints on deformation (Fig. 3A). Slender bodies can typically be represented by one-dimensional (1D) models. While pure 1D only accounts for stretching and compression, 1D models in two-dimensional (2D) space allow for curvature and bending. Such approaches are valuable to describe curvature dynamics of elongated structures, such as filaments, rows of cells, flagella, cilia or plant stems (Brokaw, 1971; Bastien et al., 2013). In contrast, epithelial layers, plant leaf epidermis or other flat tissues are often approximated as 2D surfaces. These are captured well by 2D continuum models (Tlili et al., 2015) or discrete vertex models based on junctions and vertices, which are largely inspired by foam physics (Honda and Eguchi, 1980; Nagai and Honda, 2001; Farhadifar et al., 2007). Similarly, 2D representations can be embedded in three-dimensional (3D) space to account for tissue curvature, as seen during gastrulation in *Drosophila* embryos (Streichan et al., 2018). On curved surfaces, even homogeneous stresses can trigger highly complex shape changes and, conversely, changes in curvature directly feed back into internal stress distributions (Santos-Durán et al., 2024; Tallinen et al., 2016; Gehrels et al., 2023). Importantly, dimensional reduction can also arise from symmetries and invariances in the system. For example, the growth of a perfectly spherical tissue can be described by a single variable, the radius. In contrast, systems lacking geometric constraints or exploitable symmetries require complete 3D

descriptions using multiple parameters. This applies to 3D cell aggregates, tumor growth (Messal et al., 2019; Okuda et al., 2015) and complex geometries ranging from mammalian organs to plant meristems (Savin et al., 2011; Boudon et al., 2015). Importantly, utilizing reduced dimensional descriptions (e.g. rods, shells or surfaces) is not merely a technical simplification; instead, it defines the dominant deformation modes accessible to the biological system. These modes represent the mechanically preferred pathways through which tissues drive large-scale morphological transformations. Selecting the appropriate dimensionality is therefore an essential modeling decision, as it determines which mechanical degrees of freedom are retained and, consequently, which morphogenetic processes the model can capture.

Boundary constraints

Boundary constraints act as a crucial second layer of control in tissue morphogenesis. Developing tissues are rarely isolated; they interact mechanically with surrounding structures such as the ECM, neighboring tissues, substrates or confining envelopes. These constraints are implemented in models and can trigger physical instabilities and symmetry-breaking events that would not occur otherwise, providing a possible route to pattern formation (Fig. 3B). For example, a confined growing tissue builds internal stress, which can lead to buckling, a phenomenon observed during vertebrate airway and gut development (Li et al., 2011; Shyer et al., 2013). This mechanical behavior contrasts with free boundaries, which allow simple expansion. Boundaries can also be active and/or motile, which can, for example, lead to bulk flows. At the single cell scale, cortical surface contractions powered by the actomyosin cortex can drive consistent cytoplasmic streaming (an intracellular cytoplasmic flow), as seen in the mouse oocyte (Yi et al., 2011; Wang et al., 2020a; Dehapiot et al., 2021). At the tissue/embryo scale, apical contractions in epithelial layers covering the yolk can similarly drive tissue and yolk flows, as observed in the *Drosophila* embryo (He et al., 2014; Polyakov et al., 2014). More broadly, boundary conditions in a mechanical model can dictate displacement (e.g. fixed or sliding boundaries), stress (e.g. imposed tractions, which refer to the mechanical forces that living cells exert on their immediate microenvironment), or represent complex adhesion and friction behaviors with surrounding media (Tlili et al., 2019).

Spatial heterogeneities

A central feature of developmental systems is that tissues are rarely spatially homogeneous. Spatial patterning – through gene expression, signaling gradients or cell polarity – can translate into spatially heterogeneous cellular activity and material properties (Fig. 3C). For example, differential contractility between the apical and basal surfaces of epithelial layers – a fundamental morphogenetic mechanism that occurs during embryonic development – drives tissue curvature and subsequent invagination (Lewis, 1947; Odell et al., 1981; Martin et al., 2010). At larger scales, localized active contractile regions can facilitate large-scale, non-trivial tissue flows that shape entire embryos, as exemplified by the actomyosin-driven gastrulation movements in *Drosophila* (Dicko et al., 2017; Streichan et al., 2018) and the crescent-shaped contractile patches that power embryo-scale vortex-like flows in avian species (Saadaoui et al., 2020).

Heterogeneities of growth can also elicit shape changes. Differential growth is a fundamental mechanism for controlling tissue curvature across living systems. In plants, asymmetric growth drives stem bending during phototropism and gravitropism (Lino and Briggs, 1984). In animals, cortical folding during brain

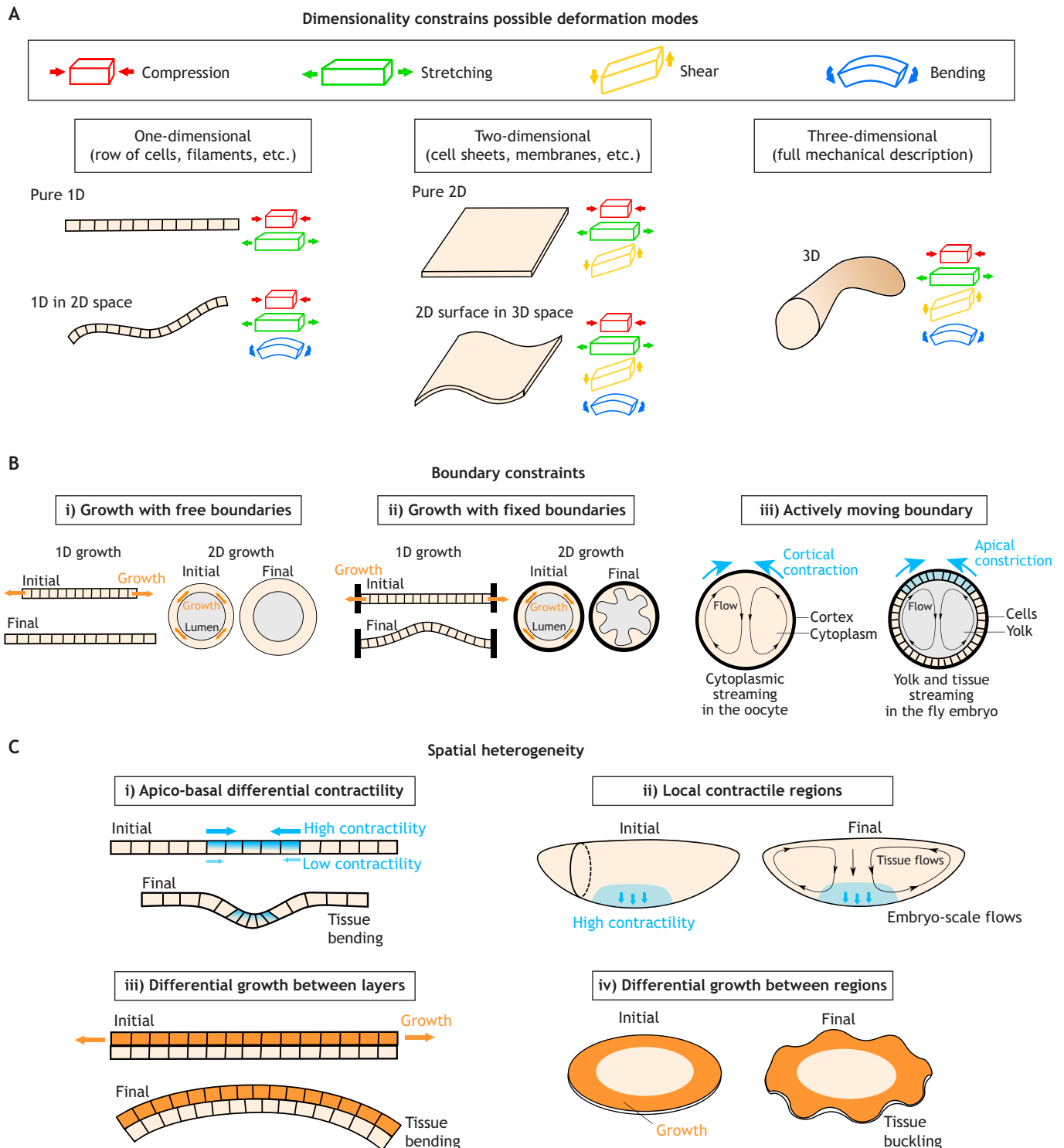


Fig. 3. Domain geometry and spatial heterogeneities guide tissue morphogenetic outcomes. (A) Constraints imposed by domain dimensionality on the possible deformation modes. (B) Boundary constraints can provide a route to pattern formation. (Bi) A row or sheet of cells growing homogeneously with free boundaries can freely expand. (Bii) A row or sheet of cells buckles if confined by fixed boundaries, and generates periodic bumps in a radial geometry. (Biii) Moving boundaries leading to passive bulk flow. Cytoplasmic streaming driven by cortical surface contractions during oocyte meiosis (left), or yolk and tissue streaming driven by surface apical constriction in the gastrulating fly embryo (right). (C) Morphogenesis from spatial heterogeneities in active force generation. (Ci) Heterogeneous distribution of contractility in cells, here apico-basal, can cause tissue-scale bending. (Cii) Localized patches of higher contractility can cause embryo-scale surface flows, as in the *Drosophila* or avian embryos. (Ciii) Differential growth between two adherent cell layers, two sides of a stem or two faces of a leaf causes tissue bending. (Civ) Differential growth between regions of an epithelium or plant leaf results in out-of-plane buckling instabilities.

gyrification (Richman et al., 1975), gut looping (Savin et al., 2011) or scales patterning (Milinkovitch et al., 2013; Santos-Durán et al., 2024) can arise from growth mismatches between adjacent tissues. In thin sheets, in-plane growth heterogeneities can be accommodated by out-of-plane buckling (Audoly and Boudaoud, 2003), which creates the complex, rippled morphologies seen in plant leaves and petals (Liang and Mahadevan, 2009, 2011).

Additionally, spatial patterning of tissue material properties constrains morphogenesis. Such heterogeneities may be quantitative (e.g. variations in stiffness) or qualitative (e.g. differences between elastic and viscous behavior). For example, gradients in tissue fluidity have been proposed to direct growth toward more fluid regions, which are more susceptible to irreversible deformation. Notably, such directional morphogenesis can emerge even when the initial driving inputs are homogeneous and isotropic, such as turgor pressure in plants (Trinh et al., 2021) or body axis elongation in vertebrate embryos (Mongera et al., 2018).

Taken together, shape, boundary constraints and spatial patterning define the geometric context within which forces act and tissue properties manifest in biological systems. These parameters determine not only quantitative outcomes, but also the qualitative repertoire of possible deformations. Consequently, they constitute indispensable components of any robust mechanical framework for development.

Conclusion

Recent years have seen a rapid expansion of approaches in developmental mechanics and their application to morphogenesis. As presented in this Primer, we are now equipped with tools to measure forces, quantify material properties and build mechanical models that capture tissue dynamics using general physical principles. Although comprehensive quantitative mechanical characterization remains limited to a relatively small number of model systems across both animals and plants, integrated biophysical approaches are becoming increasingly accessible (Sugimura et al., 2016; Campàs, 2016). The field has reached a point where such knowledge and methodologies in biomechanics can apply beyond specialized laboratories and become part of the standard toolkit of developmental biology.

However, this shift calls for a simultaneous evolution in training. To succeed, future researchers must seamlessly blend biological and physical descriptions of living systems, making interdisciplinary education essential to the future of developmental biology.

Despite substantial progress in our understanding of developmental mechanics, major challenges remain. First, the relationship between genes and mechanics is proving to be more intricate than initially anticipated. Genetic programs regulate force generation and material properties, but mechanical cues also feed back into gene expression through mechanotransduction pathways (Vining and Mooney, 2017). Such mechano-chemical feedback loops can amplify spatial heterogeneities, generate non-linear behaviors, and either stabilize or destabilize tissue forms (Hannezo and Heisenberg, 2019). More generally, feedback between tissue deformation and cellular behavior provides a potential mechanism for developmental robustness: by allowing cells to sense local mechanical states and adapt their contractility, proliferation, differentiation or growth accordingly, tissues can compensate for perturbations and converge toward reproducible morphogenetic trajectories despite variability in genetic, cellular or environmental conditions. Acquiring quantitative evidence for such mechanical canalization remains a challenge. Robustness is also likely to emerge from the reciprocal coupling between biochemical patterning and tissue mechanics. Morphogen

gradients regulate growth, contractility and cell fate, but are themselves reshaped by tissue deformations, cell rearrangements and advective tissue flows, which transport morphogens and the cells reading them. Such coupling may help maintain coherent spatial patterning while coordinating tissue-scale deformations, providing an additional layer to achieve robustness.

Second, bridging molecular, cellular and tissue-level descriptions into unified frameworks capable of predicting morphogenesis from fundamental principles remains a major challenge. Moving forward, the field requires not only improved measurements, but also frameworks that unify genes, forces, material properties and geometry into predictive theories of morphogenesis across scales. This need for multiscale integration is also widely emphasized in recent literature (Collinet and Lecuit, 2021; Lenne et al., 2021).

Beyond deepening our understanding of development, the principles that govern morphogenesis may inform the design of synthetic tissues and adaptive materials (Kim et al., 2021; Matejčić and Trepát, 2023; Jones et al., 2021; Siéfert et al., 2019). Harnessing mechanical cues to guide self-organization opens the possibility of bio-inspired engineering structures that exploit, rather than suppress, the feedback loops that are inherent to all living systems.

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Competing interests

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