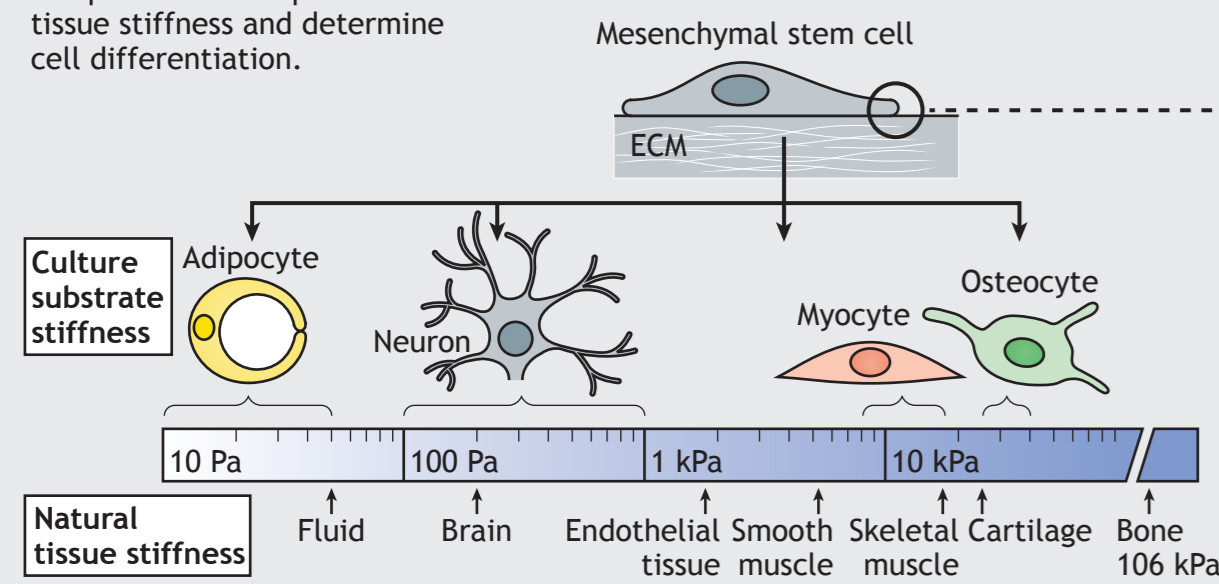


Integrin adhesion complexes

Substrate stiffness determines stem cell lineage

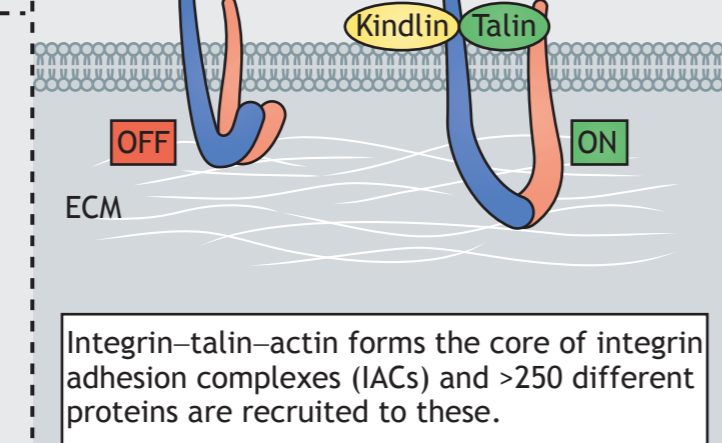
Cells sense the ECM through integrins, which form adhesion complexes that respond to tissue stiffness and determine cell differentiation.



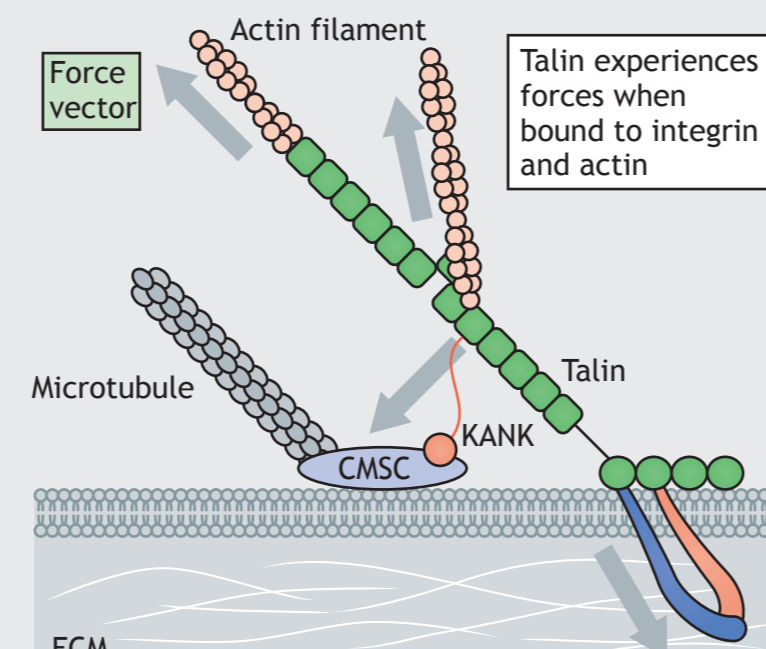
Integrins are ECM receptors

Integrin activation

Talin converts integrins into the high-affinity conformation able to bind ECM

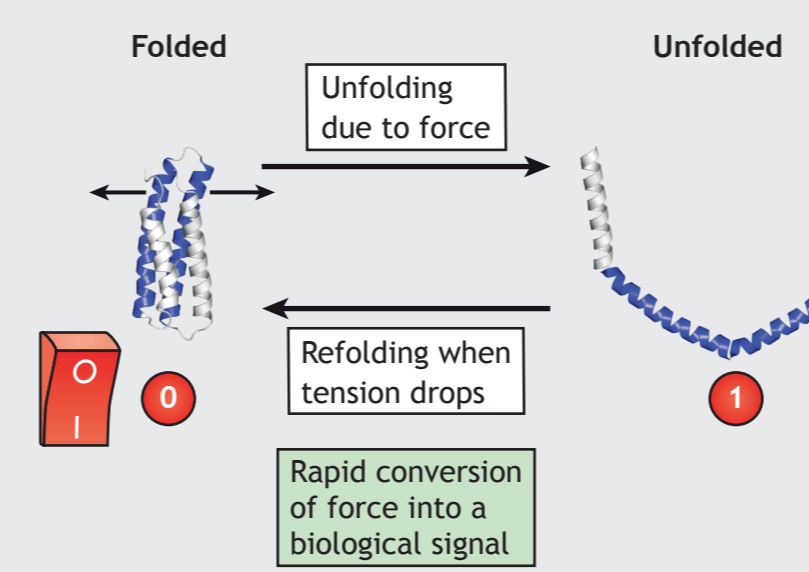


Talin couples the ECM to the cytoskeleton

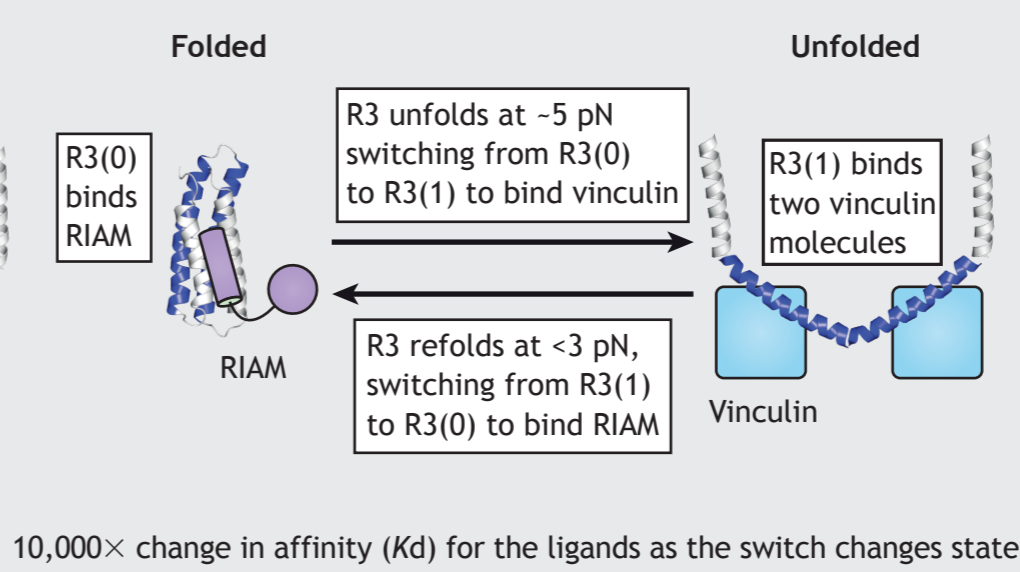


Mechanochemical switches

A mechanical binary switch

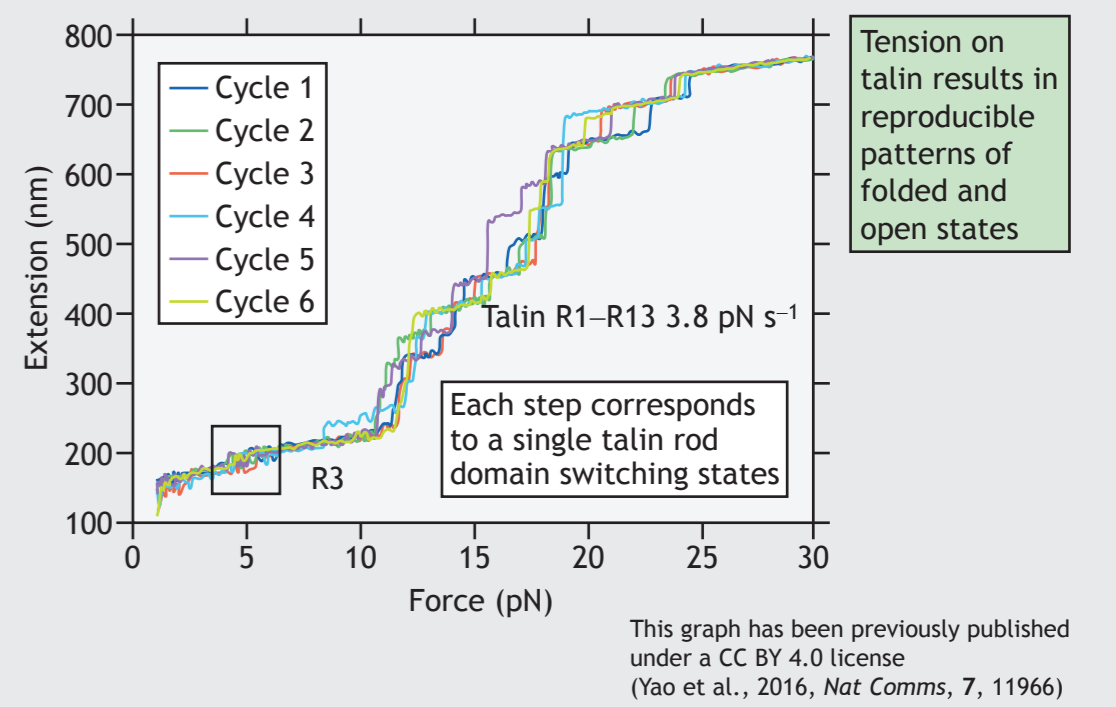


Talin R3 as the paradigm of a force-dependent binary switch

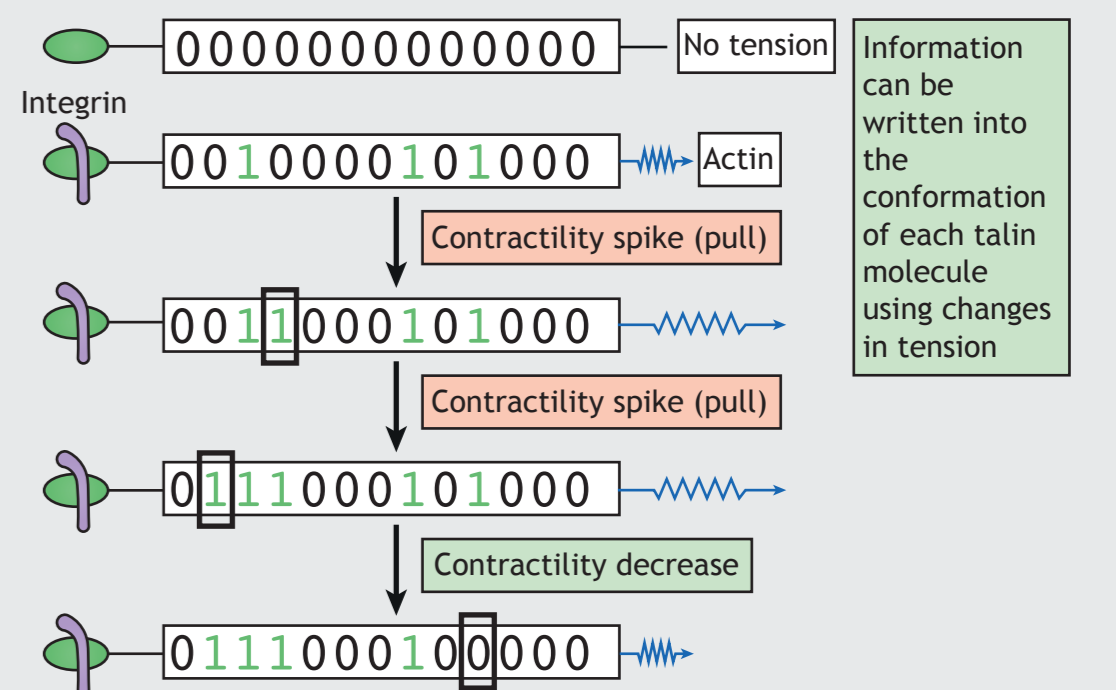


The talin code

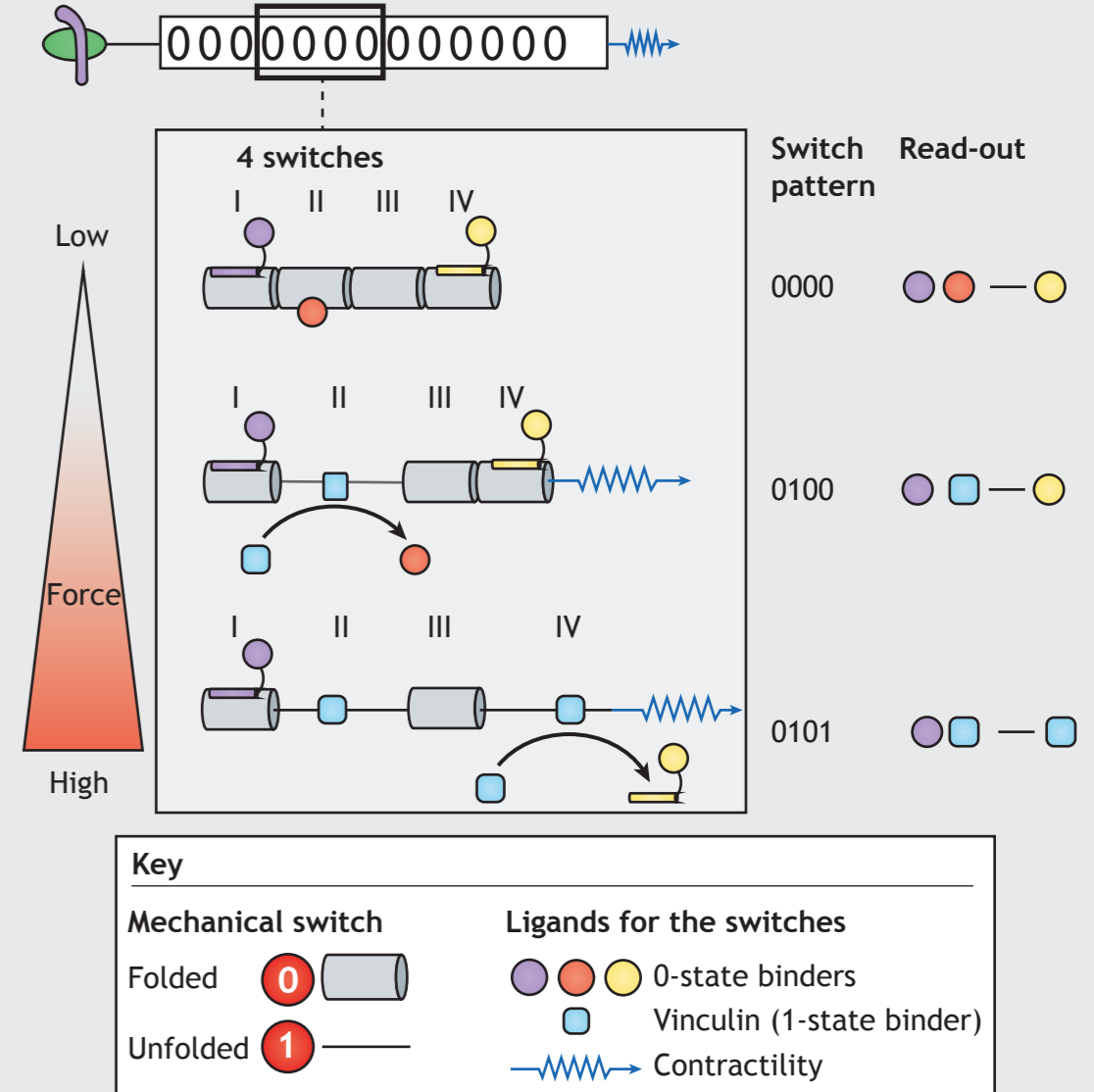
The mechanical response of talin



Talin as an information-storing molecule



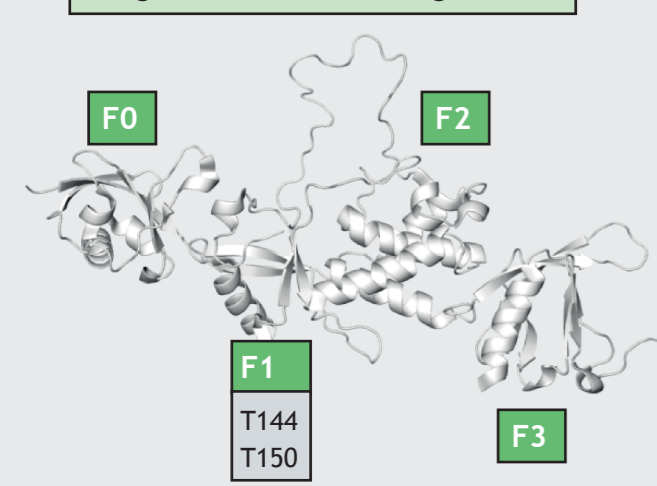
The talin switch patterns control signalling outputs



Talin structure and binding partners

Talin head domains

Talin head binding partners control integrin activation and regulation



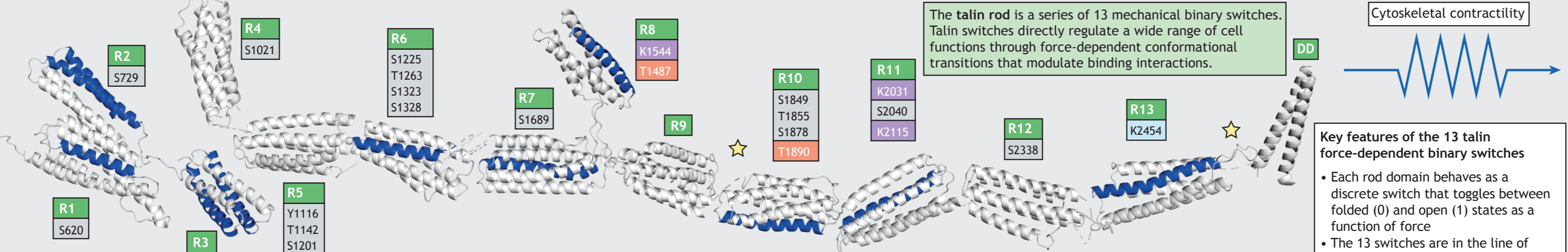
Binding partners of talin head domains

F0	F1	F2	F3
Rap1	PIP ₂ Rap1	PIP ₂ Actin	Integrin Layilin FAK Gα13 Talin PIPK1γ90

Key

	Vinculin-binding site (VBS)		Phosphorylation
	Calpain cleavage site		Acetylation
			Glycosylation
			Methylation

Talin rod domains



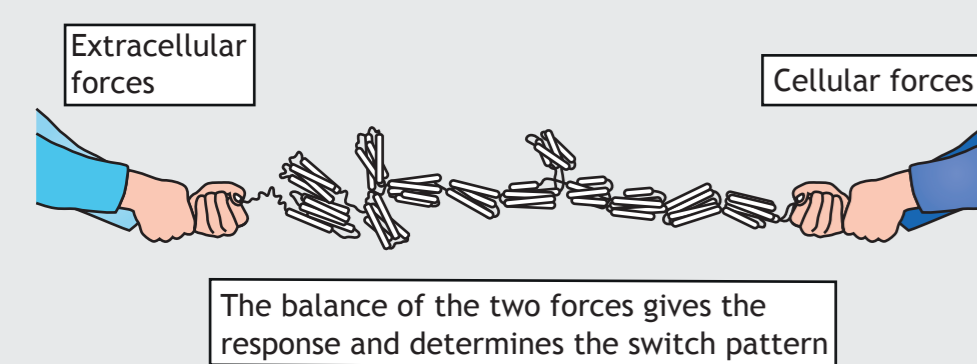
Key features of the 13 talin force-dependent binary switches

- Each rod domain behaves as a discrete switch that toggles between folded (0) and open (1) states as a function of force
- The 13 switches are in the line of force transmitted between integrins and F-actin
- Each switch opens and closes at distinct force thresholds
- Each switch binds different ligands, generating different signalling outputs
- Both the folded and unfolded states are stabilised by positive feedback loops, conferring mechanical memory
- Release of tension resets switches back to the folded 0 state

Hypothesis: adhesions as memory modules and information-processing centres

Switch operation by mechanotransduction

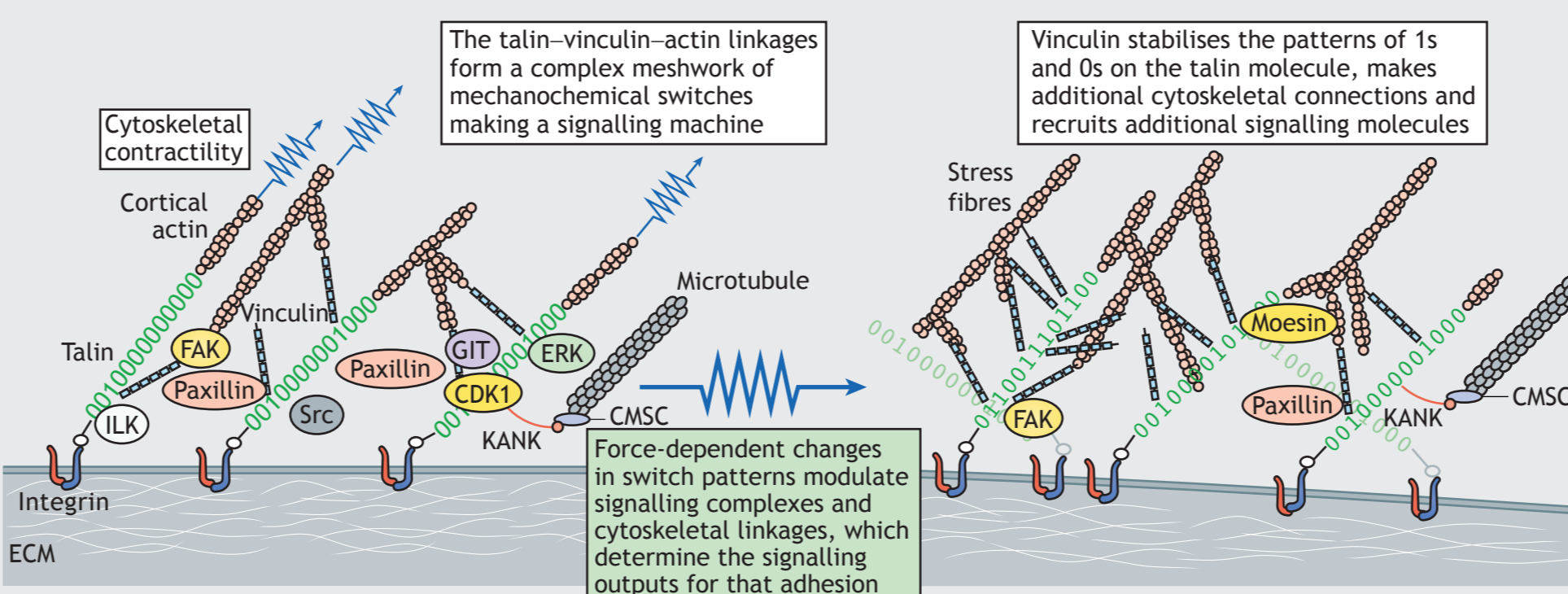
Talin is in a tug-of-war between extracellular forces and cellular forces



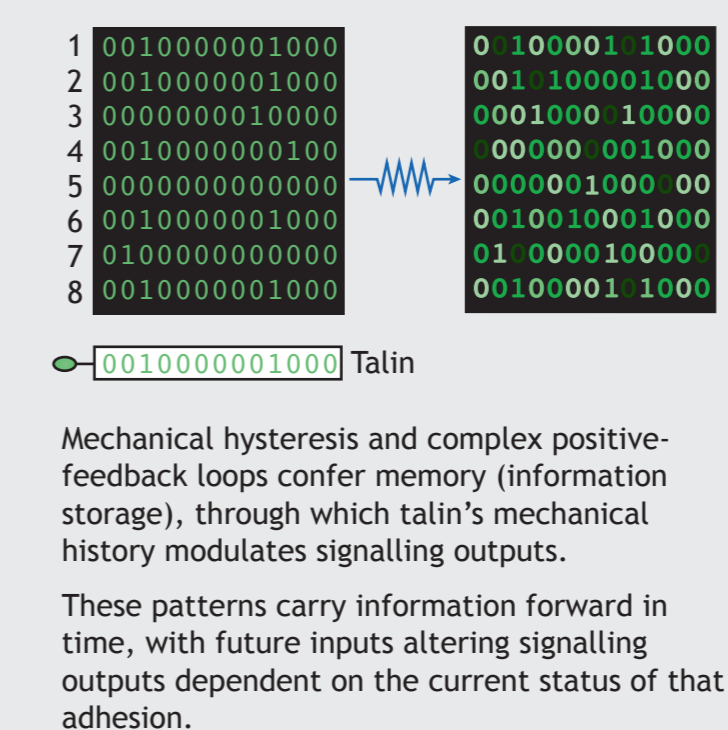
Switch operation in data storage

If the outside environment is constant, the cell can generate forces internally to control the switch pattern

MeshCODE



Example: array of eight talins



Possibility of logic gate operations

