

Filamin-A

A flexible link inside cells

Two actin-binding ends

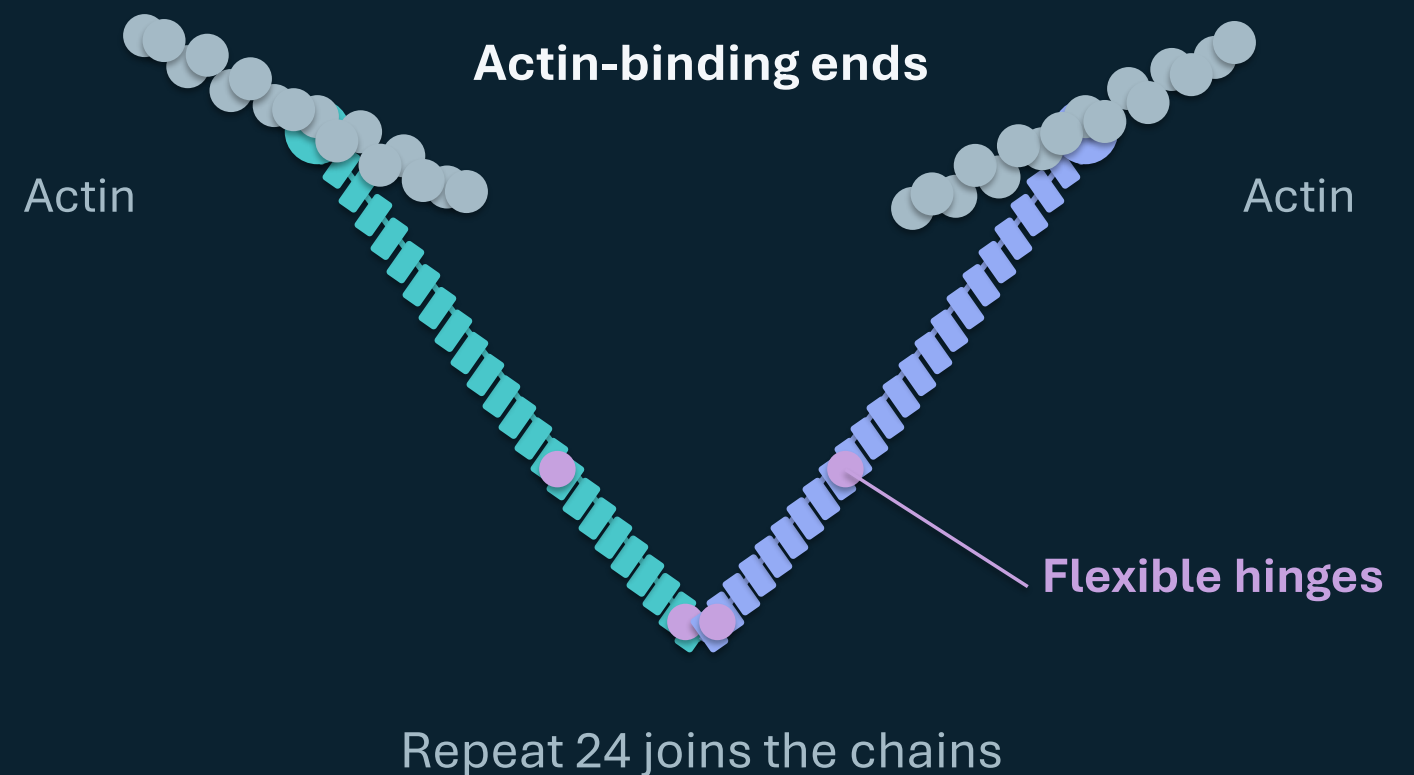
Connect different actin filaments

24 folded repeats per chain

Provide surfaces for binding partners

Flexible hinges

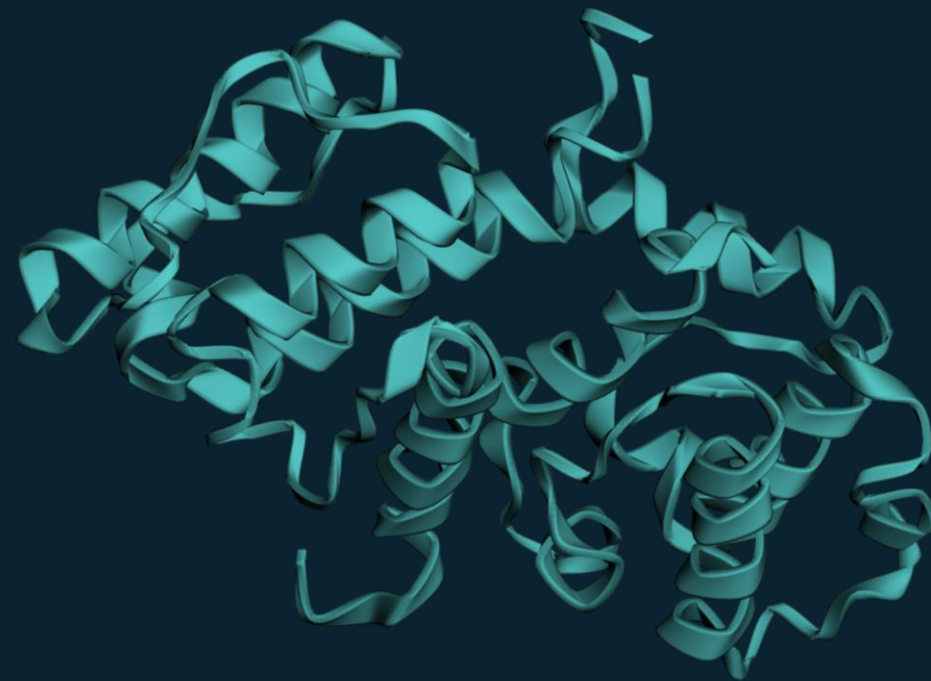
Let the network change shape



A connected network that can deform without becoming rigid.

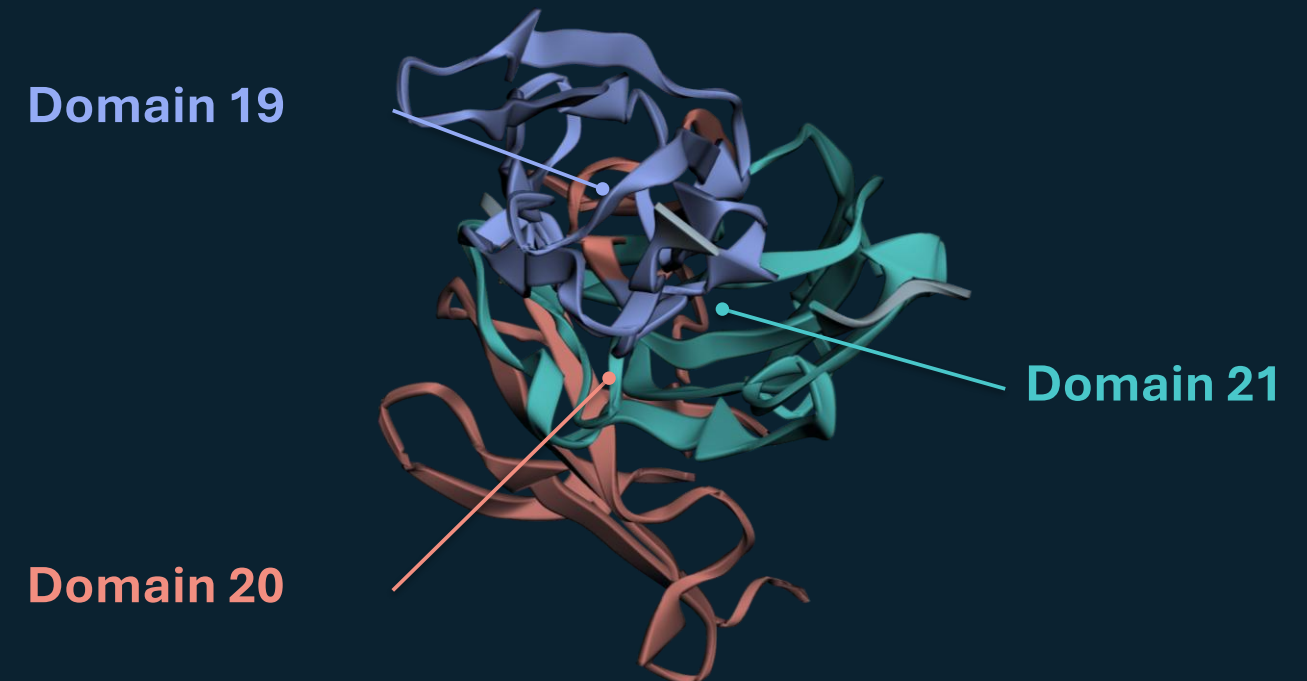
What the folded protein looks like

Actin-binding fragment



Alpha-helix-rich

Domains 19-21 (fragment)



Domain 19

Domain 20

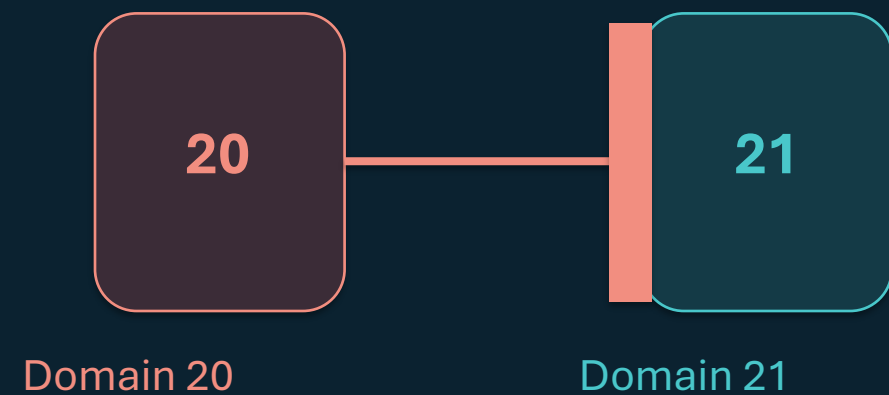
Domain 21

Beta-sheet-rich

Folding positions chemical groups for selective, reversible binding.

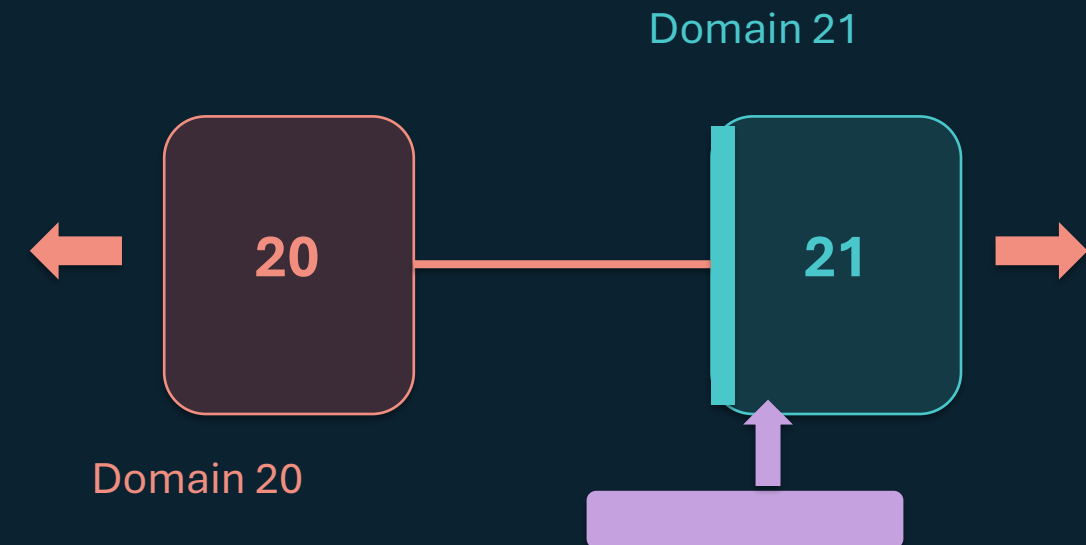
Support that can sense force

Partly masked



Binding site covered

Under tension



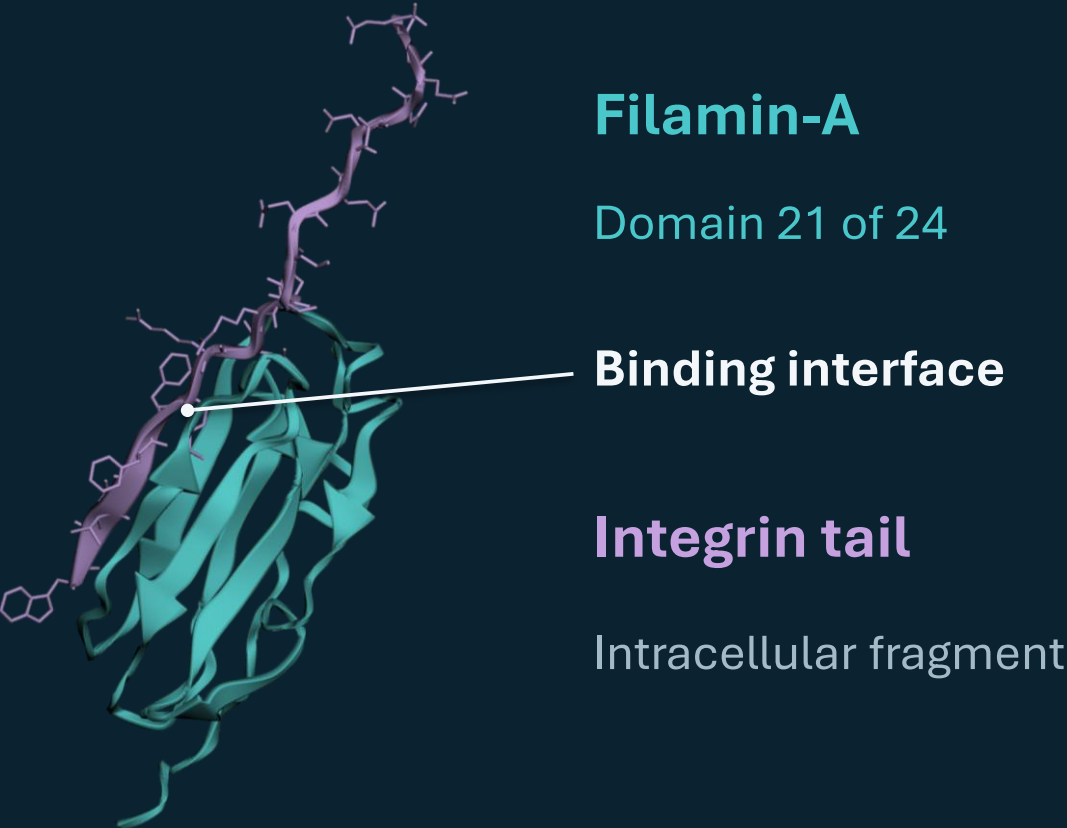
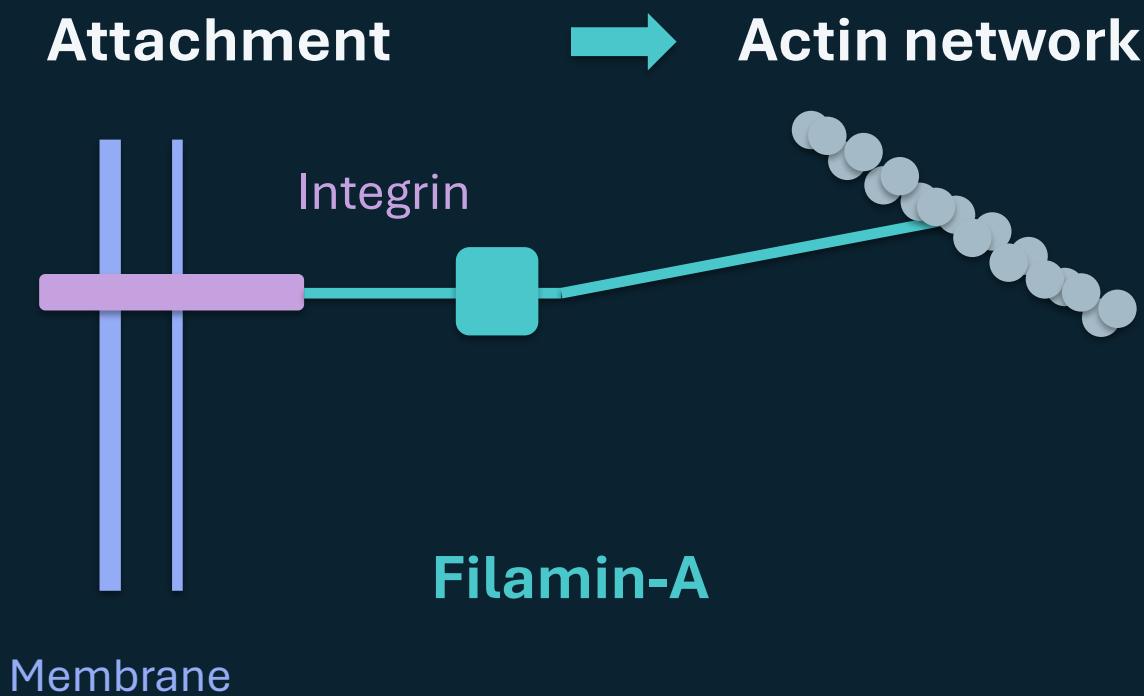
Partner can bind

Domain 20 partly covers domain 21's binding site.

Mechanical force changes molecular binding: mechanotransduction.

A working example: platelets

In a platelet



Separate binding sites connect the receptor to actin.

When Filamin-A changes

FLNA variant

Altered protein function

Disrupted tissue organisation

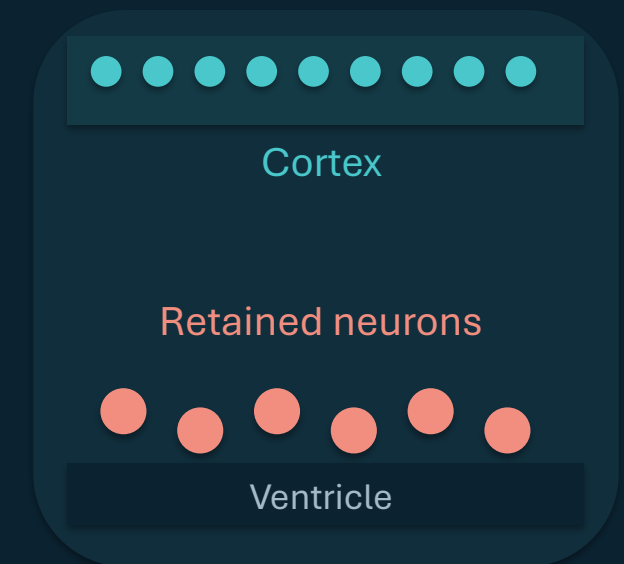
Periventricular nodular heterotopia

Neurons near the ventricles; possible seizures

Usual location



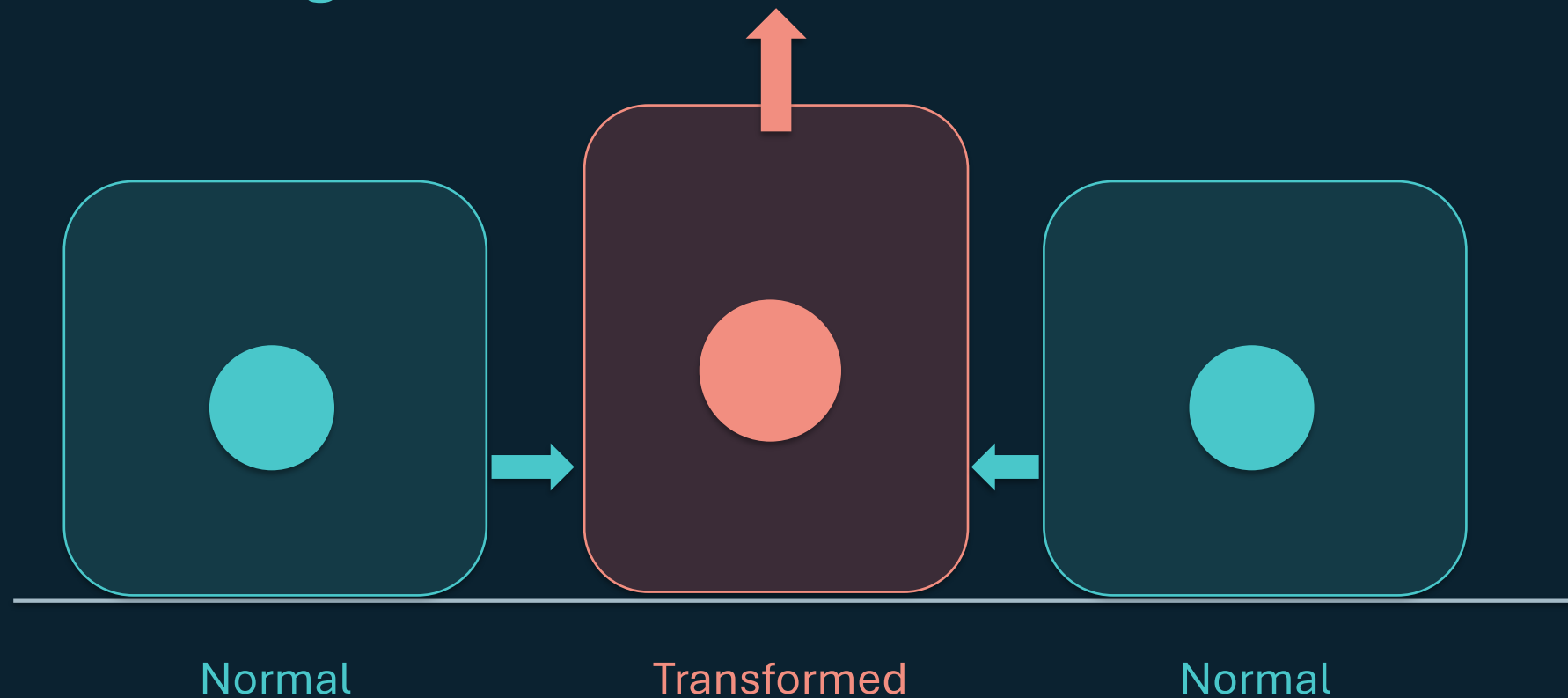
Heterotopia



Laboratory: Western blot (~280 kDa) | Clinical: MRI + genetic testing

Sensing an abnormal neighbour

Normal neighbours sense deformation



Gene-regulatory
response

Extrusion from
the cell layer

Cell-culture evidence, not an established cancer treatment.

Thank you

