

## Supramolecular architecture explains the incredible strength of fibrin blood clots

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A new study unlocks the previously unknown structural features that underlie the incredible elastic resilience of fibrin, the main protein in blood clots. The research, published by Cell Press in *Biophysical Journal* on May 18th, provides insight into how the molecular architecture of a fibrin network contributes to its resilience and may help to explain what causes the failure of a clot, which can lead to a stroke or heart attack.

Fibrin is a <u>fibrous protein</u> which assembles into a remarkably strong spider web-like gel that forms the structural framework of blood clots. Previous work has shown that fibrin networks, thought to be among the most resilient proteins in the natural world, stiffen when deformed and become increasingly resistant to further strain. Although this extraordinary resilience appears to be crucial for the biological function of blood clots, the <u>molecular basis</u> of this resilience is not well understood.

"To better understand the superior elasticity of fibrin networks, we measured the mechanical behavior of purified fibrin gels on multiple scales," says senior study author, Dr. Gijsje H. Koenderink from the Biological <u>Soft Matter</u> Group at the FOM Institute AMOLF in The Netherlands. "We found that the fibrin has a series of molecular domains that are stretched out sequentially, on smaller and smaller scales, when clots are deformed. This stretching leads to gel stiffening, which protects the clots from damage"

Specifically, Dr. Koenderink's group made the surprising discovery that



the fibrin fibers are very porous loose bundles of thin filaments that are connected by flexible crosslinkers. This open structure (containing 80% water) makes the fibers 100-fold more flexible than previously thought, and enables sequential stiffening due to straightening out of the bundles between network crosslinks followed by straightening out of flexible protein domains inside the bundles. "We found that it is this bundle-like structure of fibrin fibers that is ultimately responsible for the superior mechanical properties of fibrin gels," explains Dr. Koenderink.

The researchers presented a theoretical model that explained their observations in terms of this unique hierarchical architecture of the fibers. "Our data reveal molecular design principles that allow <u>blood</u> clots to recover from large forces, such as shear forces from blood flow, furthering our understanding of how pathological alterations in fibrin cause clot rupture and bleeding or thrombosis," concludes Dr. Koenderink. "Moreover, our findings suggest a new design concept for resilient bio-inspired materials with potential applications in drug delivery and tissue repair."

## Provided by Cell Press

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