

BUILDING AN ATOMIC STRUCTURE OF FIBRIN FIBERS USING MULTI-SCALE MOLECULAR MODELING

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Fibrinogen is a soluble protein that present in a blood plasma in large quantities. During the trauma, fibrinogen is converted to fibrin — major building block of a blood clot. Fibrin polymerizes in several steps. First, appear the short oligomers, later — bigger fragments called protofibrils are built. Protofibrils are then aggregate into the fibrin fibers. Later are fortified by numerous covalent cross-links and organize them-selves into a three-dimensional network, called fibrin gel. This network is capable of catching erythrocytes, blocking the blood flow. Pathologies in the structure of fibrin molecules, protofibrils, fibrin fibers and fibrin gel can lead to both excessive thrombosis and blood loss.

To understand the function of the blood coagulation system, detailed knowledge of the structure of its parts is required, including knowledge on the structure of fibrin polymers. Nevertheless, atomic structure of the fibrin fibers is still unknown. All the attempts to get this structure are limited to the two-dimensional picture, but the protofibrils and fibrin fibers resemble a three-dimensional helical shape.

Using the available crystal structures of fibrin molecule and its parts, we were able to reconstruct the atomic models of fibrin oligomers and protofibrils. During this reconstruction we have used a multi scale molecular modeling approach, that included molecular dynamics in full-atomic resolution, coarse-grained modeling and Monte-Carlo simulations. All the obtained structures are in good agreement with available experimental data, such as AFM and TEM pictures, small angle X-Ray scattering data, data on the single-point mutations and its influence on the function of the fibrin.