ESRF EXPERIMENTAL REPORT: Investigation of packing of protofibrils inside fibrin fibers in gel for blood clot dissolution therapy

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Our experiments show, for the first time, the existence of an high degree of lateral order in fibrin fibres on unperturbed wet samples.

In Fig. 1 a plot of the scattered intensity distributions I(q), collected at ID02 beamline, for an aged fibrin gels is reported in 400mM NaF solution.

Results reported in Fig. 1 directly confirm that protofibrils closely associate giving rise to a well known crystalline-axial packing at ∼22.3 nm [1] and to a crystalline-equatorial packing at ∼18 nm [2].

Furthermore we show, for the first time, evidence of a crystalline lateral order of protofibrils within fibrin fibres, in an unperturbed wet sample, with characteristic distances of ∼7.5 and ∼5.6 nm.

These results confirm and extend the structure predicted by the multibundle model [3].

We also investigated structural modifications (in the absence of any external perturbation) induced by varying the Cl- concentration in the gelling solution since specific binding of Cl- to fibrin monomers and oligomers is the most

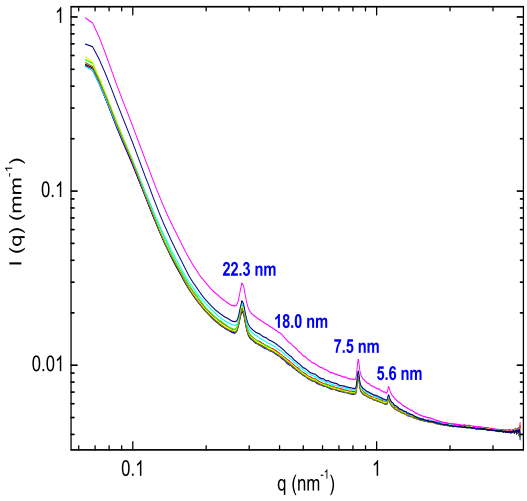

FIG. 1:

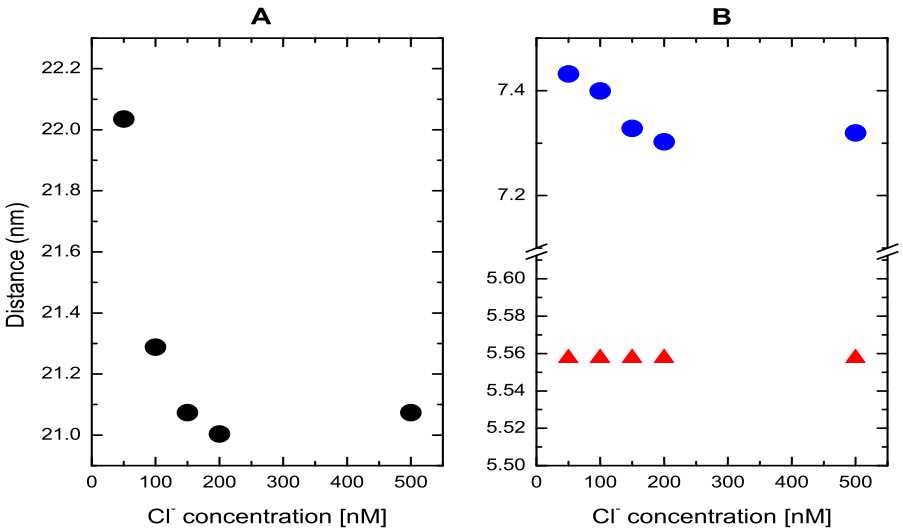

FIG. 2:

important physiologic regulator of fiber thickness, mainly acting by impairing lateral aggregation of protofibrils.

In Fig. 2A and in Fig. 2B plots of the axial peak and the equatorial peaks position respectively as a function of Cl- concentration for aged fibrin gels are reported. As evident from Fig. 2A and B peaks at $\sim$ 22 nm and $\sim$ 7.5 nm appear to be influenced by the Cl- ionic concentration while the peak at 5.6nm seems unaffected by the environment ionic strength. This last results is a clear landmark allowing to associate this characteristic distance to the lateral protofibril-protofibril distance. Indeed osmotic pressure influences the gel structure in water most accessible regions or where water shows weak bonds to proteins.

References

[1] Stryer L. et al. Nature (1963) 197, 793-794

[2] Caracciolo G. et al. Thromb Haemost 89, 632-636 (2003)

[3] Yang Z. et al. PNAS (2000) 97, 14156-61