PETERSBURG NUCLEAR PHYSICS INSTITUTE NAMED BY B.P. KONSTANTINOV
OF NATIONAL RESEARCH CENTER "KURCHATOV INSTITUTE"

Mechanisms of action for the supramolecular drugs: neutron study

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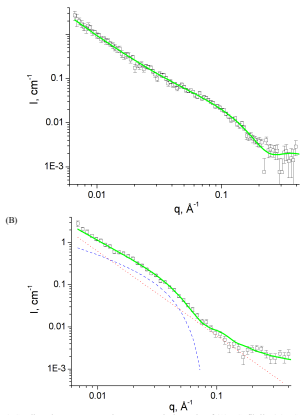
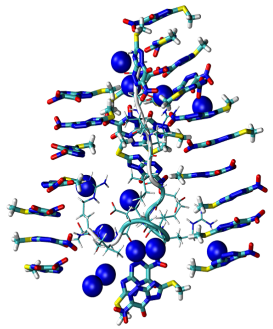
1. Low molecular weight compounds Many low molecular weight compounds and peptides are capable of forming supramolecular complexes. In the form of such complexes, the molecules are capable of multicenter cooperative binding to target proteins. It is advisable to study these complexes using small-angle scattering methods in combination with molecular dynamics modeling in the free diffusion approach.

When studying the mechanism of interaction of a triazavirin drug with polypeptides by neutron small angle scattering methods in combination with molecular dynamics, it was shown that the drug molecules are capable of forming linear supramolecular complexes and altering the quaternary structure of proteins [1]–[3].

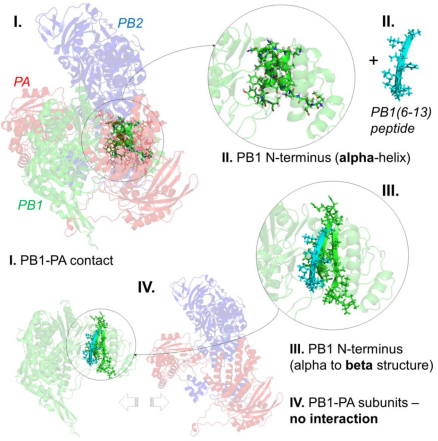


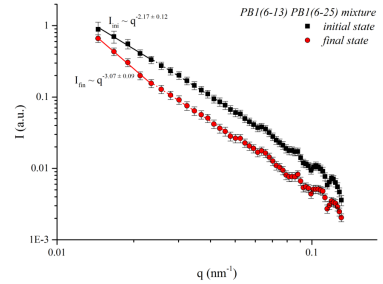
Small-angle neutron scattering curves analysis results of (A) – SI fibrils; (B) – SI fibrils with triazavirine. Data fitted to (A) worm-like model with fibril radius of 1.40 ± 0.04 nm and Kuhn length of 12.0 ± 0.7 nm ($\chi 2 = 0.83$, solid green line in Panel A) and (B) linear combination of random coil model (dotted red line) and long cylinders with the radii of 4.66 ± 0.14 nm (dashed blue line), $\chi 2 = 1.2$, shown in solid green line in Panel B.

Interactions between SI and TZV supramolecular complexes: MD simulation



2. Supramolecular amyloid-like peptide complexes are capable of specific effects on the secondary structure of the protein, which can be used to create a new class of antiviral drugs, as was shown using small-angle neutron scattering and time-resolved x-ray scattering [4]–[6].





The PB1(6-13) and PB1(6-25) peptide mixture system initial (t = 0) and final (t = ∞) states spectra, reconstructed on the basis of a change in the singular decomposition zero and first components fro TR-SAXS SVD analysis

- **Some drugs act only in the form of supramolecular complexes that are in dynamic equilibrium**
- **Existing of such complexes cannot be detected using traditional methods - chromatography or microscopy**
- **Only methods of light scattering, neutron scattering and X-ray scattering can be used in determination of its mechanism of action**

3. The interaction of supramolecular complexes formed in lipid membranes with receptors can be used to modulate cell signaling, including the creation of immunomodulating drugs that affect T cells. The effect of complexes on the chromatin structure can be used to create a new class of drugs - epigenetic regulators that affect gene expression [7].

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