

The Crystal Structure of the Rat Synapsin I C Domain Bound to Ca²⁺ and ATP

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Introduction: Synapsins are a group of proteins that have important regulatory functions in synaptic vesicular trafficking. These proteins, which account for nearly 10% of all proteins at the synapse, are found coating the synaptic vesicles. At least five different synapsins have been characterized in mammals. Comparisons of all of the mammalian synapsins has revealed that these proteins are comprised of several conserved domains. All synapsins share the C (or central) domain, which is structurally similar to a family of ATP-utilizing enzymes and is known to bind to ATP *in vitro* [1].

Results: In this study, we have used selenomethionine-containing crystals and MAD methodology to solve the crystal structure of the rat synapsin I C domain bound to Ca²⁺ and ATP. The structure is very similar to that of the bovine C domain, but some additional features are present in the rat structure. Several protein loops that were disordered or poorly ordered in the bovine structure are clearly visible in the present structure. Among these loops is a fifteen-residue span that interacts with the bound ATP and other nearby residues. This loop apparently restricts the egress of ATP from its binding site, and obviously could be very important for ATP binding *in vivo*. Also revealed by this and related crystal forms (four are available for rat synapsin I C domain) is the fact that this protein forms a well conserved tetramer.

Conclusions: Our studies thus far have illuminated the fact that a flexible loop interacts with bound ATP and that synapsin forms crystallographic tetramers. Both of these discoveries can be experimentally assessed to ascertain whether or not they have a bearing on ATP binding.

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References:

[1] L. Esser, C.-R. Wang, M. Hosaka, C.S. Smagula, T.C. Südhof, and J. Deisenhofer. "Synapsin I is Structurally Similar to ATP-utilizing Enzymes." The Embo Journal, **17**, 977, 1998.