Some fossil scorpions reached substantial sizes. The identity of the Lower Devonian *Praearcturus gigas* is finally confirmed as a scorpion, making it the largest known species, reaching lengths of 1 metre. Although this species, together with *Brontoscorpio*, which approached the same dimensions, occur in terrestrial sediments, they are too large to have moulted on land, and must have been amphibious if not aquatic. The earliest unequivocal terrestrial scorpion is *Palaeopisthacanthus* from the Upper Carboniferous Mazon Creek biota of Illinois in which stigmata are preserved (Rolfe, W.D.I. *Spec. Vol. Syst. Assn* **15**, 146; 1980). Carboniferous coals yield much scorpion material, and the unique hyaline layer in scorpion cuticle may enhance its preservation potential compared with that of other arthropods (Bartram *et al. J. geol. Soc. Lond.* **144**, in the press).

Kjellesvig-Waering's work reveals striking similarities between the preabdominal morphology and respiratory structures of aquatic scorpions and those of eurypterids, and indicates that these two groups are closely related. This supports recent classifications that no longer group the eurypterids with the xiphosurids in the class Merostomata, but recognize that the Xiphosura is the primitive sister group of other chelicerates (for example, Weygoldt, P. & Paulus, H.F. *Z. Zool. Syst. Evolut.-forsch.* **17**, 177; 1979). □

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Cell biology

Synapsin I and the cytoskeleton

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IN THE search for clues to the mechanism of nervous transmission, proteins associated with structures at synaptic termini are being probed in ever-increasing detail. At the focus of much effort is synapsin I, a protein associated with small synaptic vesicles. Recent results from several groups are now coming together to form the basis for a mechanism of synaptic transmission. The debate will be further stimulated by the observations of M. Bähler and P. Greengard, reported on page 704 of this issue[1], describing an actin-bundling activity associated with synapsin I. This bundling activity is efficiently expressed only by the dephosphorylated form of synapsin I — on phosphorylation, catalysed by protein kinases activated by nerve depolarization, the activity is lost.

Synapsin I, first discovered by Greengard and colleagues as a substrate for cyclic AMP-dependent protein kinase, seemed to be one of the major substrates for that kinase in the brain. It subsequently became clear that it is also a substrate for calcium/calmodulin-dependent protein kinase and protein kinase C. Most excitingly, though, phosphorylation of synapsin I appeared to occur on depolarization of nerve endings (see ref. 2 for a review). Experiments in which synapsin I in known phosphorylation states was injected into the presynaptic side of the squid giant synapse suggested that synapsin I is involved in the regulation of availability of synaptic vesicles for exocytosis[3]. Thus dephosphorylated synapsin I might 'restrain' synaptic vesicles in a way that could be overcome by phosphorylation in response to depolarization.

What type of restraint could this be? One possibility is that dephosphorylated synapsin I holds synaptic vesicles in a cytoskeletal meshwork. If so, phosphorylation would release the vesicle for exocytosis. Bähler and Greengard's observations, then, come in the context of several reports suggesting interactions with cytoskeletal components. Synapsin I apparently interacts with brain spectrin (fodrin)[4-6], and the three major classes of cytoplasmic filament: microtubules[7,8], neurofilaments[8,9] and F-actin[1]. All these interactions occur *in vitro* with moderate affinity (dissociation constants in the range 0.5–5 μM). One further activity of dephosphorylated-synapsin I is that it enhances the binding of spectrin to F-actin[10], an activity paralleling that of the erythrocyte membrane-bound protein 4.1, with which it has some limited antigenic cross-reaction[4,5].

The relationship between synapsin I and actin is perhaps less surprising in view of the recent discovery[11] that small regions of the synapsin sequence are 40–50 per cent identical to villin, a calcium-dependent actin severing and bundling protein, and profilin, a protein that sequesters actin monomers. The polymerization reaction demonstrated by Bähler and Greengard is similar to that of profilin under the same conditions. Although Bähler and Greengard have no evidence for an actin-sequestering activity, this is a point that bears re-examination. Equally, it is not clear how synapsin bundles actin — does it have more than one actin binding site per monomer or are monovalent molecules prone to aggregate in the dephosphorylated form to give a polyvalent crosslinking structure? The dissociation constant for actin–synapsin interaction is not related to phosphorylation state, but the stoichiometry of the maximum binding changes from 11 mol actin per 1 mol synapsin in the fully phosphorylated form to 7 mol actin per 1 mol synapsin in the dephosphorylated form. Such stoichiometries are puzzling but could support aggregation as the means of crosslinking.

Where does this leave us? Because we lack detailed understanding of the cytoskeletal architecture in the presynaptic terminus, it does not yet seem possible to make a coherent model of the relationship (if any) between synaptic vesicles, the cytoskeleton and exocytosis. It should be possible, however, to make a few conjectures. Bähler and Greengard[1] argue that there is little evidence for microtubules and neurofilaments in the presynaptic terminus: indeed, where synapsin has been shown to colocalize with microtubules and neurofilaments it is in parts of the neuron other than the synapse[8]. Conceivably, then, interactions between synapsin and microtubules/neurofilaments may relate more to vesicle transport towards nerve endings than to exocytosis. On the other hand, actin is abundant in presynaptic termini and spectrin is also present. Spectrin seems to be for the most part membrane-bound, so perhaps dephosphorylated synapsin I secures the synaptic vesicle in a complex with spectrin and actin close to the presynaptic plasma membrane. It is also relevant that synapsin *in vitro* can crosslink synaptic vesicles to membranes[9] and that affinity of synapsin I for synaptic vesicles is reduced by phosphorylation[9,12]. In this view, nerve depolarization would cause an elevation in free cytosolic calcium activating a calcium/calmodulin-dependent protein kinase and phosphorylating synapsin, thus reducing its interaction with (or at least its ability to crosslink) the synaptic vesicle, spectrin and actin, freeing the vesicle for exocytosis. There are many objections to such a scheme, not the least of which is that synaptic exocytosis occurs extremely rapidly on depolarization. But it seems reasonable to suggest that at the very least synapsin I is involved in positioning synaptic vesicles close to the plasma membrane in a cytoskeletal lattice or meshwork before exocytosis. □

1. Bähler, M. & Greengard, P. *Nature* **326**, 704–707 (1987).
2. Browning, M.D., Huganir, R. & Greengard, P. *J. Neurochem.* **45**, 11–23 (1985).
3. Llinas, R., McGuinness, T.L., Sugimori, M. & Greengard, P. *Proc. natn. Acad. Sci. U.S.A.* **82**, 3035–3039 (1985).
4. Baines, A.J. & Bennett, V. *Nature* **315**, 410–413 (1985).
5. Goodman, S.R. & Zagon, I.S. *Am. J. Physiol.* **250**, 347–360 (1986).
6. Kanda, K., Tanaka, T. & Sobue, K. *Biochem. biophys. Res. Commun.* **140**, 1051–1053 (1986).
7. Baines, A.J. & Bennett, V. *Nature* **319**, 8495–8504 (1986).
8. Goldenring, J.R. *et al. J. biol. Chem.* **261**, 8495–8504 (1986).
9. Steiner, J. Ling, E. & Bennett, V. *J. biol. Chem.* **262**, 905–932 (1987).
10. Krebs, K.E., Zagon, I.S. & Goodman, S.R. *J. Cell Biol* **103**, 2829a (1986).
11. McCaffrey, C.A. & De Gennaro, L.J. *EMBO J.* **5**, 3167–3173 (1986).
12. Schiebler, W., Jahn, R., Doucet, J.-P., Rothlein, J. & Greengard, P. *J. biol. Chem.* **261**, 8383–8390 (1986).

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