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Strange Things Happen in Small Spaces: How Synaptic Vesicles Fill with Neurotransmitter

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The transport of all classical neurotransmitters into neurosecretory vesicles requires a proton electrochemical gradient ($\Delta\mu_{H+}$) generated by the vacuolar-type H^+-ATPase. Nonetheless, different transmitters rely on either the chemical component of $\Delta\mu_{H+}$ (ΔpH) or the electrical component $\Delta\Psi$. Chloride entry through ClC-type transporters has long been considered the main factor regulating expression of $\Delta\mu_{H+}$ in many cells, but we have recently identified two novel activities that influence relative expression of ΔpH and $\Delta\Psi$. These mechanisms in turn predict distinct effects on synaptic vesicle filling with different transmitters.