Minimal energy principles determine spatial localization and turn-over of molecules

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The human ability to perform a wide variety of complex cognitive tasks relies on the integrity and plasticity of the connections neurons establish predominantly via chemical synapses. Especially the post-synapse, located at neuronal dendrites, is relevant in implementing changes of synaptic strength. The molecular basis of each synapse is its specific protein content. It is, however, unclear which rules neurons follow to provide the right proteins at the right synapse, especially regarding the long dendritic distances molecules have to travel in their relatively short lifetime. We study this question with a biologically plausible mathematical model of intracellular particle dynamics which can reproduce a wide variety of experimental observations. With our model, we can show that metabolic efficiency is a major determinant shaping intracellular molecule trafficking. Specifically, we find that the localization of mRNAs, the biochemical precursor molecules of proteins, and the overall number of mRNAs and proteins follow a minimal energy principle. These predictions are underpinned by six large-scale screens of neuronal mRNAs and proteins. Our model framework can easily be extended to also incorporate plastic synapses, thereby allowing us to study the subcellular dynamics underlying synaptic plasticity.