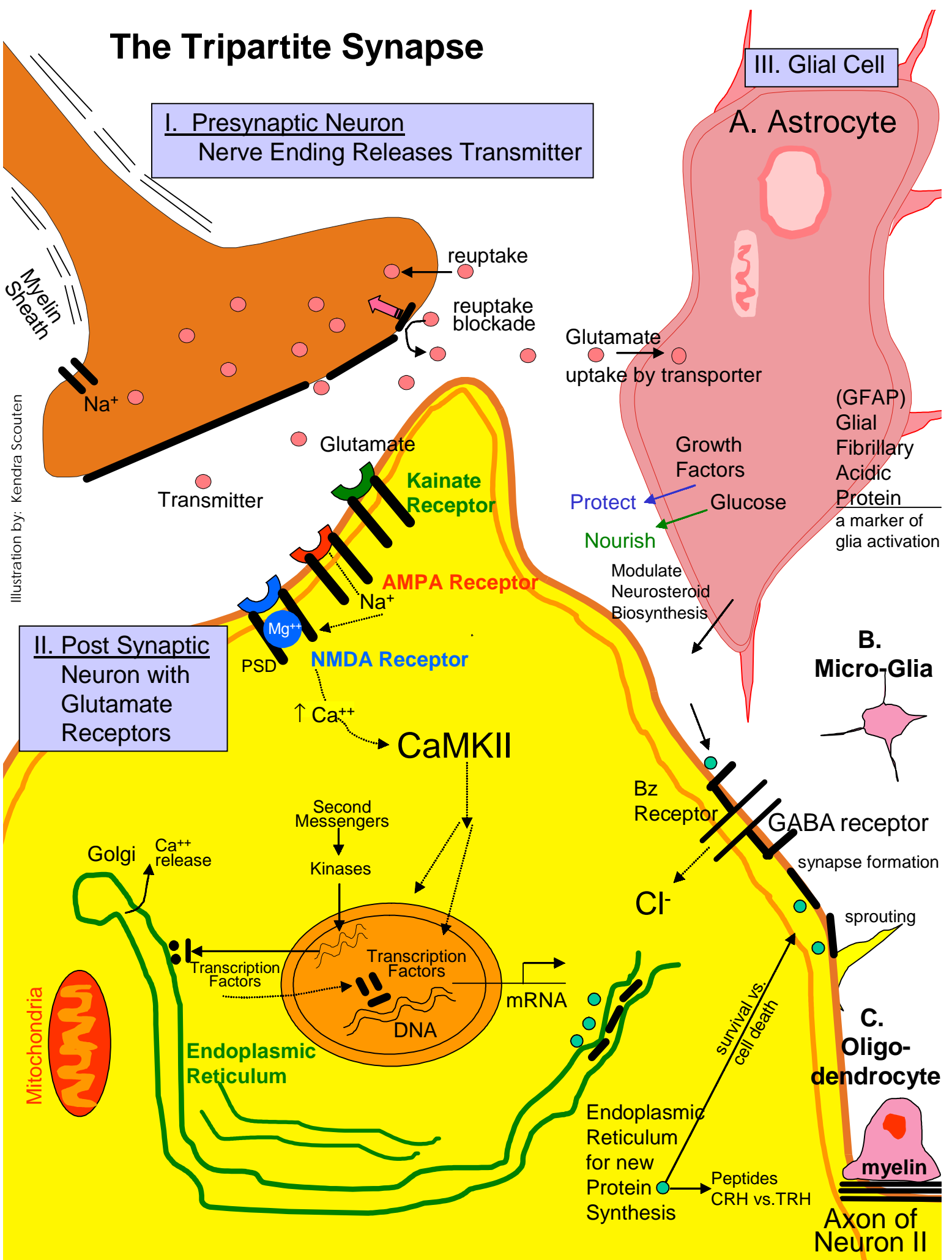


The Tripartite Synapse



Legend:

The **Tripartite** (three-part) **Synapse** involves: **I)** a **presynaptic axon** of neuron I (orange, top left) releasing transmitters to activate (glutamate) or inhibit (GABA-Bz) activity of the **II) post-synaptic neuron** (yellow, middle). The third critical component is **III) the glial cell** (pink, top right), an **(A) astrocyte** which protects cells by taking up glutamate to prevent overexcitation and secretes growth factors; provides energy via glucose; and modulates receptor (R) function with the generation of neurosteroids (which interact with Bz-GABA receptors and NMDA receptors). Other **(B) microglia** secrete cytokines and scavenge cellular debris; while **(C) oligodendrocytes** make the myelin necessary to insulate the axons of neurons to insure good conductivity. The myelin sheath breaks down in Multiple Sclerosis (MS) and now there is evidence of oligodendroglia dysfunction in bipolar illness and failure in late stages of schizophrenia. CaMK-II is the major calcium ion (Ca⁺⁺) sensor of the neuron involved in up or down regulation of synaptic excitability necessary for short and long term memory. It is decreased in bipolar illness.

The neurons (I and II) and glia (III) of parts of the prefrontal cortex appear deficient in number and function. Lithium increases the survival and production (neuro-glia genesis) of both cell types!

Abbreviations:

Na⁺⁺, sodium ion; Mg⁺⁺, magnesium; NMDA, AMPA, and kainate are three types of glutamate receptors in the postsynaptic density (PSD); Ca⁺⁺, calcium ion; CaMKII, calcium calmodulin kinase-II; GABA, gamma-aminobutyric acid; Bz, benzodiazepine; Cl⁻, chloride ion; CRH, corticotropin-releasing hormone; TRH, thyrotropin-releasing hormone.