Hydration of the Neurotransmitter γ-Aminobutyric Acid and its Isomer α-Aminobutyric Acid

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Upon release by the pre-synaptic cell, neurotransmitters (NTs) ensure unidirectional signal transport in living organisms by diffusion across the synaptic cleft connecting two neurons or joining a muscle cell and a neuron, followed by subsequent binding to an appropriate post-synaptic receptor. NT diffusion, interaction with the phospholipid cell membrane, and binding to the receptor strongly depend on NT hydration [1]. Whilst numerous investigations on NT-receptor interactions can be found, surprisingly little is known on NT-H_2O interactions. With this communication we extend our previous studies devoted to acetylcholine (a cation) [2] and glutamate (an anion with additional zwitterionic moiety) [3] to the zwitterionic NT γ-aminobutyric acid (GABA).

The extremely water-soluble (~12.6 mol/kg) GABA is the predominant inhibitory NT regulating neural activities in the mammalian central nervous system and crucial for the mental and physical health of humans [4]. This contrasts with the behaviour of its structural isomer α-aminobutyric acid (AABA), which is only moderately soluble (~2.2 mol/kg), does not act as a neurotransmitter and is thought to be of only minor pharmacological importance.

We used dielectric relaxation spectroscopy (DRS) in the microwave region to characterize the cooperative dynamics of aqueous GABA and AABA solutions up to the saturation limit. The thus obtained total effective hydration numbers, Z_t, could be split into contributions of Z_{ib} strongly and Z_s moderately bound H_2O molecules. 1D- and 3D-RISM calculations were used to locate these hydrating water molecules in the primary hydration shells of GABA and AABA, revealing fairly different hydration patterns for both solutes.

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