Histamine – a signalling cue influenced by fluctuating environmental conditions and climate change?

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Histamine, an enzymatic decarboxylation-product of the amino acid histidine and well-known for its involvement in numerous physiological processes within the human body, also serves as an external signalling cue for invertebrates. When functioning as a settlement cue for sea urchins [1] or as a foraging cue for freshwater snails [2], histamine is exposed to a range of environmental factors, such as temperature, pH and salinity. These physical conditions are subject to large fluctuations and are projected to be influenced significantly by climate change over the course of this century. In this study, we assess the sensitivity of histamine and its essential properties to current and future environmentally relevant ranges of pH, salinity and temperature.

Employing a combination of Molecular Dynamics and static DFT geometry optimisation methods, we investigate if protonation caused by a change in pH affects the molecule's conformation, charge distribution and dipole as well as interaction with surrounding ions. Multiple MD simulations were performed with parameters representing either very low or high levels of salinity equivalent to fresh or salt water and different temperatures to simulate natural temperature ranges in coastal and riverine ecosystems. We established that changes to the protonation state of histamine are small for conditions relevant in marine ecosystems, while for freshwater systems there are two relevant protonation states that dominate alternately. The two forms differ significantly in their conformation and charge distribution as well as in their interaction with surrounding Cl^- and Na^+ ions. Charge as well as conformation are key elements in receptor-ligand interactions and significant changes to these properties, as observed here, could hint at a potential disruption of histamine's signalling function for invertebrates with consequences for essential ecosystem interactions.

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