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Chemical properties emerging from structural disorder in biology

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During neurodegeneration, the first stage of neuronal death, abnormal concentrations of structurally disordered proteins and ions, like zinc and copper, are observed in the synapse. Some proteins, like amyloid-beta (Abeta) peptides, form, in the Alzheimer's disease, oligomers and aggregates that become markers of the irreversible pathway towards death. When such conditions occur in the synapses, the chemical species formed by copper and amyloid peptides produce levels of radicals comparable with the free copper ions, thus increasing the oxidative stress.
Using computational resources offered by the PRACE infrastructure, we have extensively modeled the interactions between copper ions and amyloid-beta peptides in a water environment and in contact with a model synaptic membrane. The models explain why weak Cu-Abeta interactions, specific of amyloid beta peptides, make copper more aggressive 1.
We simulated about 120 walkers starting from different configurations for one to four copper ions in contact with one to four amyloid-beta peptides, on the basis of empirical models. Each of these configurations was refined with explicit electrons, thus modeling the details of the copper-peptide interactions for all the configurations at the same time. Thousands of computing units can be
efficiently used at the same time, to provide an approximate statistical view of reactivity.
These models open a new venue for understanding, at an atomic level, the role of disordered biological molecules in making the chemistry of reactive centers versatile, a general feature of living cells 2.

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