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Evolutionary cues in the physicochemical description of proteomes

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With the glaring exception of highly conserved binding interfaces, protein surfaces tend to be regarded as variable regions of hydrophilic character, subjected only to soft evolutionary pressures. However, in crowded cellular conditions, electrostatic interactions between surfaces take on a critical role in modulating protein interactivity, with downstream consequences for protein stability, mobility and solubility. In this context, surface net charge density stands out as the single most important determinant of protein mobility inside the cell. Moreover, in *E. coli*, proteins organise around a moderately negative net charge density value, which ensures cytosol-wide colloidal stability: molecules keep away and remain highly mobile most of the time, but close-range interactions are allowed upon small thermal fluctuations. Our results show that, across organisms, the average value at which this Goldilocks situation is achieved varies, often depending on niche and intracellular conditions: extreme lifestyles—archaeal halophiles and endosymbiotic bacteria— can be mapped to different net charge density values. By combining net charge density with other simplistic physicochemical observables, derived from sequence data alone, we can show that the profile of different organism groups changes consistently with the taxonomical hierarchy. Thus, we propose that previously unrecognised evolutionary cues can be revealed by inexpensive physicochemical profiling, and that these have the potential to contribute complementary information to state-of-art phylogenetic inference.

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