Title: **Computational study of charge regulation effect on the stretching of weak polyelectrolytes**

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Date: June 2020

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Weak polyelectrolytes stretching is a flourishing research field due to the constant upgrade in the single molecule experimental techniques and the interest that the understanding of these macromolecules' behaviour awakes. For this reason, the main objective in this work is to perform a computational study about weak polyelectrolytes that allows to evaluate which relationship exists between charge regulation and mechanical stretching. In this particular case, hyaluronic acid has been chosen as the molecule of study, a natural polymer with a wide range of applications, specially in medicine and cosmetics.

This computational study is based on the implementation of a minimal theoretical model that includes the fundamental aspects that describe weak linear polyelectrolytes stretching, which are: conformational equilibrium, proton binding, bond stretching and bending, steric hinderance and mechanical work. As the analytic resolution of the model is of high complexity, it was decided that Semi-Grand Canonical MonteCarlo simulations will be used. These simulations were carried out at different pH, ionic strength and pulling force values, the latter being only employed in stretching experiments. Data obtained through simulations provides information on both conformational properties (end-to-end distance $\langle r^2 \rangle$, chain elongation L_z, persistence length l_p and Kuhn length l_k) and protonation properties (degree of protonation or coverage θ, effective acidity pK_a^{eff} and proton binding capacity C) but, above all, it provides information of the mechanisms that interrelate these properties, which are crucial to understand how charge regulation works.

Finally, a comparison is performed between the two outlines proposed to represent the hyaluronic acid macromolecule, and the differences are discussed. At the same time, while studying their behaviours, the different observed force regimes are analysed and their impact to the polyelectrolyte properties is also assessed.

Keywords: weak polyelectrolytes, coarse-grained model, MonteCarlo simulation, mechanical stretching, charge regulation, hyaluronic acid.