Tuning polypeptide multilayer growth and mechanics via solvent-mediated interactions

Maria Morga [1], Tuuva Kastinen [2], Izabella Leszczyńska [1], Piotr Bonarek [3], Jodie Lutkenhaus [4,5], Maria Sammalkorpi [2,6], Piotr Batys [1]

[1] Jerzy Haber Institute of Catalysis and Surface Chemistry, Polish Academy of Sciences, Poland
[2] Department of Chemistry and Materials Science, Aalto University, Finland
[3] Faculty of Biochemistry, Biophysics and Biotechnology, Jagiellonian University, Poland
[5] Artie McFerrin Department of Chemical Engineering, Texas A&M University, USA
[6] Department of Materials Science and Engineering, Texas A&M University, USA
[7] Research Council of Finland Center of Excellence in Life-Inspired Hybrid

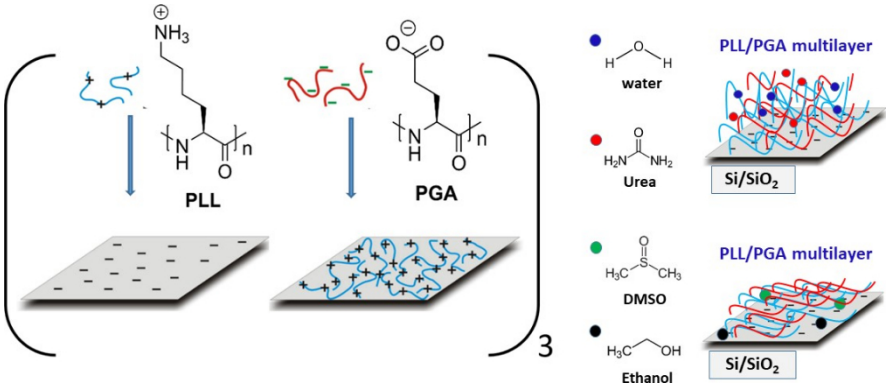
piotr.batys@ikifp.edu.pl

The use of co-solvents is a common strategy to modulate polypeptide conformation; however, their specific role in coupling charge regulation with interfacial assembly and film mechanics remains insufficiently understood. In this work, we investigate how three widely used co-solvents—ethanol, urea, and dimethyl sulfoxide (DMSO)—affect the solution behavior of poly(L-lysine) (PLL) and poly(L-glutamic acid) (PGA) across a broad pH range (3–11) at controlled ionic strength, and how these effects translate into layer-by-layer multilayer formation on silica substrates.

By combining electrokinetic measurements, spectroscopic analysis, molecular dynamics simulations, and in situ mechanical characterization, we identify distinct solvent-dependent mechanisms governing polypeptide behavior. Ethanol and DMSO primarily promote counterion condensation and partial dehydration of the polymer chains, whereas urea induces charge compensation via direct hydrogen bonding with the peptide backbone, leading to significant disruption of secondary structure.

These molecular-level effects directly impact multilayer growth and viscoelastic properties. At pH 6, where both polyelectrolytes are highly ionized, the presence of co-solvents significantly enhances multilayer buildup compared to purely aqueous conditions. Ethanol produces thin, compact, and mechanically stiff films, while urea and DMSO yield thicker, softer, and more dissipative multilayers.

Overall, this study establishes a direct link between solvent-mediated charge regulation in solution and interfacial assembly, demonstrating that solvent selection alone provides a powerful route to tailor the architecture and mechanical response of polypeptide multilayers.



Schematic of PLL/PGA layer-by-layer assembly on Si/SiO_2 in water, urea, DMSO, and ethanol.

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