Title:	Understanding anomalous mobility of proteins on SDS-PAGE with special reference to the highly acidic extracellular domains of human E- and N-cadherins
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Abstract:	During SDS-PAGE experiments, proteins generally display electrophoretic mobility in keeping with their molecular weights; however, some proteins display anomalies in mobility. Here, we focus attention on the anomalies displayed by the highly acidic ~110 residues-long, sequence-homologous, structurally-analogous, extracellular domains of human E- and N-cadherin. We report that there is a strong correlation between the acidity of each domain and the degree of the anomaly that it displays. The anomaly is only seen if the ratio of the numbers of negatively-charged and positively-charged residues is equal to or greater than the value of 1.50. The degree of the anomaly rises in proportion with this NC:PC ratio. Greater-than-expected anomalies are observed for domains containing dense clusters of negatively charged residues. A simple explanation for these observations is that highly acidic domains electrostatically repel SDS. This results in insufficient SDS binding, insufficient electromotive incentive and (consequently) lowered electrophoretic mobility. This explanation is in consonance with the current view that initial stages of SDS-protein engagement tend to be dominated by electrostatics. We discuss the current anomalies within the broader context of all conceivable explanations for such anomalies.
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