Team proposes new law to accurately measure charged macromolecules

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For biochemists, measuring the size and diffusion properties of large molecules such as proteins and DNA using dynamic light-scattering techniques and the Stokes-Einstein formula has been mostly straightforward for decades, except for one major snag - it doesn't work when these macromolecules carry an electric charge.

Now polymer theorist Murugappan Muthukumar at the University of Massachusetts Amherst has derived a solution to the 40-year dilemma, proposing a new theory that is allowing polymer chemists, engineers and biochemists for the first time to successfully apply the Stokes-Einstein law governing situations that involve charged macromolecules. Details appear in the current early online edition of *Proceedings of the National Academy of Sciences*.

As Muthukumar explains, "The ability of molecules to diffuse becomes smaller as the molecule's size gets larger, but for charged molecules, it's not true, diffusion doesn't depend on size. This was very surprising to physicists and biochemists 40 years ago when they were trying to measure charged macromolecules using light scattering. They also found that molecules of the same charge were aggregating, or clumping when they should repel each other. It was very surprising and nobody understood why."

Further, experiments showed that when the repulsion between similarly-charged molecules is made weaker by adding salt to the solution, the clumps went away, he says. "People were mystified by not being able to measure the size of these molecules accurately, and by their unusual behavior."

After a long process of eliminating possible explanations, he now understands what is happening. "It turns out that these molecules are not alone, there are small ions all around them, neutralizing the charges of the macromolecules," Muthukumar says. "These small ions are more agile and control the behavior of the macromolecules."

His paper offers formulae and testable predictions of a new theory or law governing charged macromolecules, DNA, proteins and synthetic poly-electrolytes. Experimental polymer scientists are already testing the new ideas in current investigations.

Muthukumar says this solution took him ten years to work out. "I began by simply believing the experimental facts and accepting that there must be an explanation. I started by taking a walk and asking myself, how could this be?"

As the theorist approached experimentalists with his ideas for solving the conundrum over the years, each had an objection that Muthukumar had to overcome. Finally, he reached the ion solution and heard no protest. "They have to be there," he now says. "The whole system has to be electrically neutral, otherwise you'd have an instability, which does not happen. Now we know how much the small ions are contributing. Using my formula, size of charged macromolecules can now be accurately determined using light scattering."

More information: Ordinary–extraordinary transition in dynamics of solutions of charged macromolecules, *Proceedings of the National Academy of Sciences*, www.pnas.org/cgi/doi/10.1073/pnas.1612249113

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