Sanli Faez

Assistant professor of physics at Utrecht University My current scientific activities are mainly fo[...]

Sanli Faez's Self-Journal

2016 JANUARY 08 - SINGLE PARTICLE CHARGE TRACKING - 22

Editorial

Electrophoresis is the underlying mechanism for a broad range of essential analysis techniques in colloid science, biochemistry, and biotechnology. The electrophoretic mobility (drift velocity in a viscous medium under application of external electric field) of proteins and other macromolecules is a very sensitive indicator of their internal charge state, their interaction with the surrounding environment, and their hydrodynamic radius. As such, it has been used for sorting a mixture of macromolecules or studying their conformational changes due to chemical reactions or physical adsorption to other molecules. Capillary- and gel- electrophoresis are two of the most widely used methods of measuring electrophoretic mobility in ensembles of molecules.

These methods, however powerful, are too slow for following the temporal dynamics of a kinetic reaction. In the existing devices, the smallest measured sample volume (in the nanolitre range) is limited by the optical detection sensitivity. This minimal volume still contains millions of molecules and each molecules proceeds on a stochastic and unsynchronized path throughout the reaction. While statistical methods can be used to uncover the reaction rates for simple processes, this is a daunting task for multi-step reactions.

In an ensemble measurement, the observation of intermediate states is often impossible because of averaging over unsynchronized and inhomogeneous processes. This is why single molecule studies have played a very central role in uncovering the intermediate steps of biomolecular and catalytic reactions. Single particle measurements are not prone to disturbance by impurities because these event can be singled out in data analysis. Furthermore, such measurements can be repeated as many times as necessary for collecting reliable and informative statistics. In other words, when the physicists' granular view of a reaction on a single particle is reconstructed by a direct measurement, the characteristic kinetics and thermodynamics of the reaction is no more obscured by material inhomogeneities or stochastic dynamics over the metastable intermediate states. Important chemical reactions, such as photo-catalysis or enzyme-catalysis, involve multiple steps of largely differing timescales. Furthermore, their reaction rates can be heterogeneous within an ensemble of catalyst particles and can even vary over time for a single catalyst particle. In principle, there is no fundamental barrier for studying a full chain of chemical reactions on a single molecule or nanoparticle through monitoring its electrophoretic mobility, IF (and that is indeed a big IF) one could track the single molecule motion BOTH on the shortest necessary timescales AND as long as the reaction is complete.

Actually, in a glorified experiment more than a century ago, Robert Millikan and Harvey Fletcher mastered measuring the drift velocity of a floating charged particle continuously to a level that they could set an accuracy record for the value of the elementary charge. The challenge we still face is how to perform that measurement on a single particle or even a single molecule, rapidly enough for resolving the reaction steps. The significance of reaching this goal is self-evident: if a researcher can monitor the charge (or the electrophoretic mobility) of a single solute rapidly enough, she or he will be able to study kinetic interactions such as ionization, hydrolysis, or charge transfer at the single particle level. In such a measurement, one can directly "track" the intermediate steps of a reaction, which are smeared out in bulk experiments because each molecule follows its own pathway stochastically.

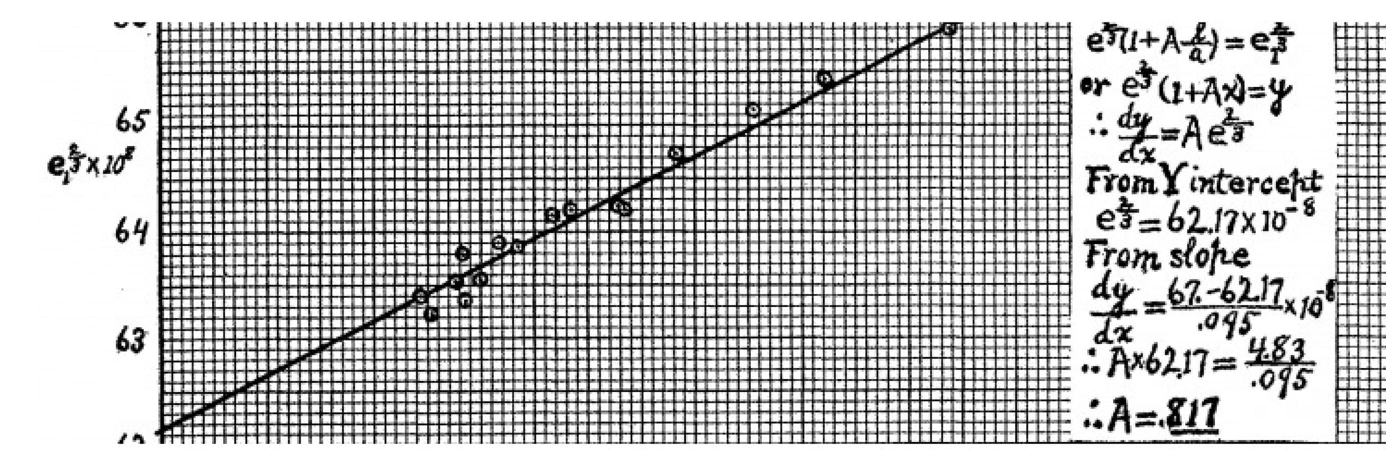
In this issue, I comment on a handful of experimental reports that, in my view, together make a convincing case that monitoring chemical reactions on mobile nanoparticles and single molecules is within experimental reach. I start with Millikan's 1911 article in the Physical Review where he presented his (or their, more on this later) first measurements of charges on a single oil droplet. Next comes the anti-Brownian (ABEL) trap developed by Cohen and Moerner which teaches out how to shrink the size of the probed particle to the nanometer scale and to perform the experiment inside dense fluids. In this 100-year fast forward, I skip all the remarkable developments around trapping single atoms and single electrons in vacuum inside quadropole traps with the excuse that those are passive, while Millikan and Cohen trap particles in their setups by using an active (visual) feedback. Another recent experiment by Beunis et al, performed in a passive optical trap, reconfirms elementary charge sensitivity of drift velocity measurements now in dense inorganic fluids, albeit on micrometer size dielectric particles. On a parallel token, I take a beautiful demonstration of sensitivity of capillary electrophoresis to elementary charge differences, here in ensembles of proteins, in the group of Whitesides. The fringe contrast of these charge ladders, limited mostly by the finite size of the measured sample, testifies to sufficient durability of charges in such biomolecules well below the elementary charge fluctuation. These results also signify the importance of long-duration measurements for monitoring charge fluctuations. Short duration of mobility measurement, due to photobleaching, and coarse time resolution, due to the limited photon budget, are the two major limitation of the ABEL trap for monitoring such chemical reactions that I envision. This is inherent to any technique that is based on fluorescence detection. I conclude this issue with one experimental report on particle tracking based on elastic light scattering and a feasibility study for performing equivalent of Millikan's experiment with small nanoparticles and even some macromolecules.

Colloids | Electrophoresis | Electrochemical reactions | Single molecule manipulation | Nanoscale thermodynamics | Nano-optics | Microscopy

SANLI FAEZ

Curator's comment

The oil droplet experiment is so famous that it hardly needs any introduction. Replicates of this setup are commonly used for practical training in physics courses. Meteorological descendants of Millikan's apparatus, still working on the same principles, are still in use for discovery of fractional charges at ambient conditions. The main reason for the longstanding avail of this method is probably its elegant simplicity: by observing the drift velocity of a particle forced by an external electric field one obtains its electrophoretic mobility, which has usually a well-defined relation with the net charge of the particle. This article in the Physical Review is not the first report on Millikan's efforts for measuring the charge, nor it is the one in which he reported the most precise value of the fundamental charge up to his time. The latter was published two year later in 1913. In this article however, the use of oil droplets (instead of water) were presented, and it contains a very thorough and didactic discussion of the measurements. Only if Millikan have had given Harvey Fletcher the proper credit that he truly deserved.



EXTERNAL LINK

The Isolation of an Ion, a Precision Measurement of its Charge, and the Correction of Stokes's Law

04 / 01 / 1911

Robert A. Millikan

No Abstract

Priority (0) Reviews (0+0)
Curators (1) Discussions (0+0)

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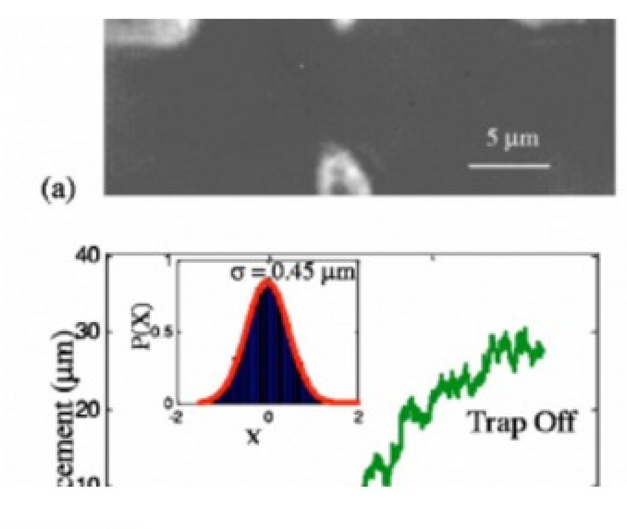

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Method for trapping and manipulating nanoscale objects in solution

25 / 02 / 2005

Adam E. Cohen — W. E. Moerner

We present a device that allows a user to trap a single nanoscale object in solution at ambient temperature, and then to position the trapped object with nanoscale resolution. This anti-Brownian electrophoretic trap (ABEL trap) works by...

Priority (0) Reviews (0+0)
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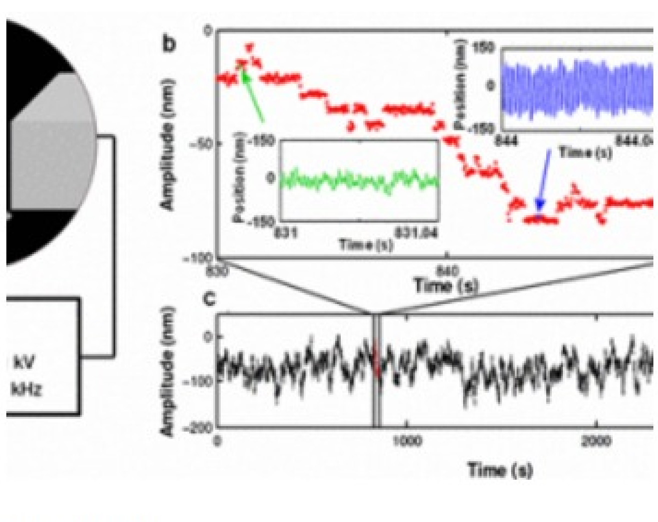
Curator's comment

A century passed before Adam Cohen and W E Moerner finally demonstrated that it is possible to apply the same technique on much smaller particles or even single molecules inside dense fluids. In this paper in Applied Physics Letters they report their technique applied on relatively "large" particles (20 nm)...



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Beyond Millikan: The Dynamics of Charging Events on Individual Colloidal Particles

01 / 06 / 2012

Filip Beunis — Kristiaan Neyts — Filip Strubbe — Dmitri Petrov

By measuring the stable charge on oil drops in air, Millikan demonstrated the discrete nature of electric charge. We extend his approach to the charge on solid-liquid interfaces, and focus on the dynamics of the discrete fluctuations....

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Curators (1) Discussions (0+0)

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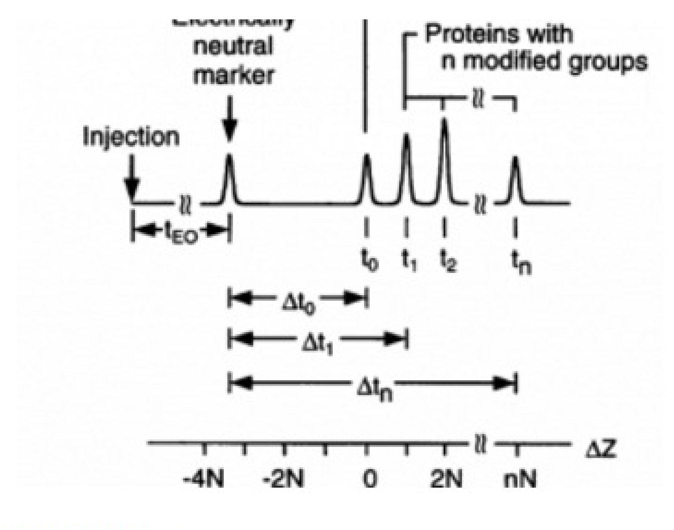
Curator's comment

The imaging speed limitation can be lifted if one uses elastic scattering instead of fluorescence emission as the signal. A beautiful demonstration has been done by Beunis and coworkers in this experiment where they use an optical tweezers for holding the particle...



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Determination of the effective charge of a protein in solution by capillary electrophoresis

12 / 06 / 1994

J. Gao — F. A. Gomez — R. Härter — G. M. Whitesides

This paper describes two methods to estimate the effective charge of a protein in solution by capillary electrophoresis and demonstrates these methods by using representative proteins. In one method, a "charge ladder"–a series of...

Priority (0) Reviews (0+0)
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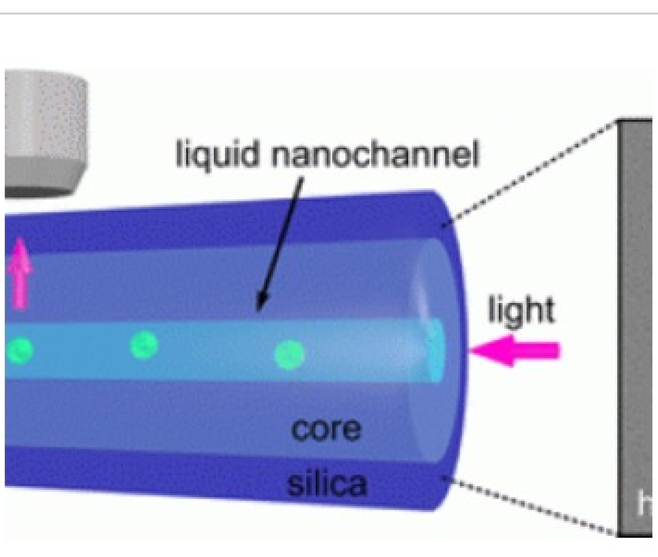
Curator's comment

The main difficulty of sensing single charges in aqueous solutions in the high solubility of ions due to the polarity of water molecules. The relevant length scale is the Bjerrum length, which is the separation at which the electrostatic interaction between two elementary charges is comparable in magnitude to the thermal energy...



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Fast, Label-Free Tracking of Single Viruses and Weakly Scattering Nanoparticles in a Nanofluidic Optical Fiber

27 / 10 / 2015

Sanli Faez — Yoav Lahini — Stefan Weidlich — Rees F. Garmann — Katrin Wondraczek — Matthias Zeisberger — Markus A. Schmidt — Michel Orrit — Vinothan N. Manoharan

High-speed tracking of single particles is a gateway to understanding physical, chemical, and biological processes at the nanoscale. It is also a major experimental challenge, particularly for small, nanometer-scale particles. Although...

Priority (0) Reviews (0+0)
Curators (1) Discussions (0+0)

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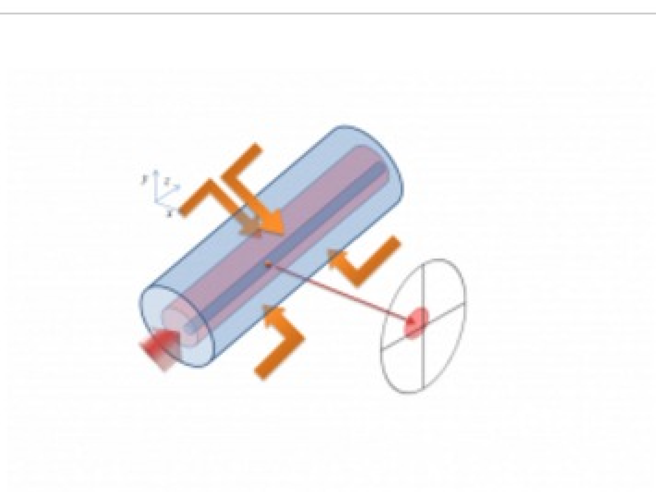
Curator's comment

How can we measure the charge ladder with just a single protein? In principle, this should be possible in the ABEL trap, but the duration of the measurement needs to be very long (maybe several minutes) for all the reactions to take place. So far I do not know of any dye molecule that can emit fluorescence for so long...



Research project

How to replace the oil droplet in Millikan's experiment with a single virus

Deposited on 06 / 01 / 2016

Sanli Faez

A highly sensitive optical capillary electrophoresis measurement method based on a nanofluidic optical fiber platform is presented. By using scaling arguments and considering realistic instrumental limitations, I underline the...

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Curators (1) Discussions (0+0)

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Curator's comment

I close this issue with a simple feasibility study of measuring charges of very small objects or macromolecules by combining the ABEL trap with the nano-fluidic fiber platform presented before. Using elastic light scattering is, in my point of view, the key to this measurement because such a long and high bandwidth measurements on a single nanoparticle must be non-dissipative...