Mini Review

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Journal of Nanoscience & Nanotechnology Research

2021
Vol. 5 No.1: 13

Shadow of Electron Beam for Plumbing at Molecular Level

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Citation: KV Chinmayaa (2021) Shadow of Electron Beam for Plumbing at Molecular Level. J Nanosci Nanotechnol Res Vol.5 No.1:13

Abstract

Do you know how a tall tree consumes water from the root and transports water and other nutrients to the top of the tree? It is because of the huge pressure difference between the underground water and the top of the tree caused by the nano-metric channels. Nature always shows quite fascinating nano-channels in day-to-day life. Such molecular transports are some of the fundamental reasons behind life on earth. Nature is optimally designed for plumbing at that molecular level. Nanofluidic devices are one such device to identify and understand the flow of single molecules. In this research article published in the Lap on a Chip by the Royal Society of Chemistry a team of researchers goes close to nature's ability to handle individual molecules. In this brief review, we highlight the importance of Lap on Chip devices with recent applications. In this review, the scientists showed how to use subatomic particles, like electrons, to manufacture such tiny nanochannels and identify the flow of individual single molecules inside them in a liquid phase.

Keywords: Nano fluidic; e-beam lithography; Feynman-Enderlin path; Fluorescence; Electro osmosis

Abbreviations: EBL: e-Beam Lithography; SAEBD: Shadow Angle e-Beam Deposition; LoC: Lab on Chip; UNLoC: Universal Lab-on-chip; LC-TEM: Liquid Cell Electron Microscopy.

Received: August 27, 2021; **Accepted:** September 10, 2021; **Published:** September 17, 2021

Introduction

The flow of a nano-meter small single organic molecule, less than two-nanometer small graphene quantum dots, and 11 nano-meter DNA molecules were achieved by movement of liquid in response to an applied electric field across the nano-channel (Electro osmosis) which takes place continuously in all living cells. The team could perform the same inside these artificial nano-channels at a single-molecule level, which was possible due to their newly developed nano-fabrication method. It is difficult to keep the molecules inside a volume for detection in the liquid phase because of the random movement of the particles in a defined medium and sorting small bio-molecules with a single-molecule level resolution is as challenging as capturing the movement of dust motes in a room. In recent years, nanofluidic devices have played a significant role in the investigation of DNA optical mapping, single virus, and nano-particle detection [1-5]. The method of investigation on the dynamics of single-molecule diffusion inside a nano-metric confined volume will be easy when increasing the sensitivity of the nano-channel neglecting the Debye's length [6].

Literature Review

In this study, the researchers fabricated the silica nano-channels which have the cross-sectional diameter ranging from 30 nanometer to 100 nanometer (30×10^{-9} to 100×10^{-9} meter) which the human eye can't measure [1]. To create enclosed nano-channels, the first method is to fabricate open nano-channels or trenches using e-Beam Lithography (EBL) followed by reactive ion etching, and finally, closing them using Shadow Angle e-Beam Deposition (SAEBD). This allowed them to understand the one-dimensional flow and diffusion of single molecules, such as small DNA molecules by detecting their fluorescence, using two-focus fluorescence correlation spectroscopy. This report presents a

dynamic single-molecule nanofluidic detection method at the length scale where molecular interactions can be influenced by surface charge and dielectric confinement for photo-physical artefacts.

The major advantages of this device are early detection of lung cancer protein-misfolded-diseases (Alzheimer's), and pathogen-mediated respiratory diseases (COVID-19/TB) are crucial due to limited therapeutics. The early detection of these diseases is very important [7-14]. If we know the detrimental entities, we should not encourage till it gets transmission into humans. The question remains, can we not detect them as early as in the air/water at ultra-low concentrations? Similarly, understanding the degradation of clean energy producing nano-materials at an early stage (atomic-resolution) in the ambient will certainly decelerate climate change. The common problem in these imperative fields is the unavailability of a robust/universal/low-cost tool that can handle single-molecules, single-virus, and single-nanomaterial's of our interest in `fluid' at nano-metric level i.e., not impossible to achieve. Peer-reviewed studies demonstrated them, but they are not democratically available.

Nanofluidic is a flourishing field in nanotechnology. It opens up the multitudinous fundamental questions in physics, chemistry, and biology. Nano fluidics is also a multidisciplinary meeting place, where researchers from many fields such as hydrodynamics, condensed matter, statistical physics, chemistry, materials science, structural biology, and so on should gather to combine distinct perspectives and take this field forward. The new ideas like has the potential to bring the Universal single-molecule sensitive nanofluidic Lab on Chip (LoC) that is compatible to all electron/optical microscope are not present in the market [1]. The current closest commercial nanofluidic products are non-universal/restricted solutions and expensive, their business interest is either in the optical microscopy market or electron microscopy but not universal. Currently, a correlative study using the same chip in electron as well as optical microscopy is not allowed. The problems are also prone to produce bulging structures at the electron transparent region due to the pressure difference. The bulging effect increases the thickness of the fluid and reduces the resolution electron's free path and resolution. The fundamental building blocks of lab-on-a-chip like Universal Lab-on-chip (UNLoC) and the field of lab-on-a-chip are academically well explored and established.

Liquid Cell Electron Microscopy (LC-TEM) is a one-power tool to visualize molecules in motion. The field is still at its infancy [15]. It has recently emerged as a powerful method to investigate processes in the liquid phase with nano-meter scale resolution. Through the use of specially designed cells and carefully controlled electron doses, even radiation-sensitive biological materials can be investigated. Recent advances in liquid cell design are bringing the grand challenge of detecting molecular motion during biological [16-18]. These nanofluidic devices also have a potential impact on structural biology. Liquid cell electron microscopy is taking another level of research in Nano fluidics now. Over the past few decades, the LC-TEM has shown a sudden gush of interest from generating advances thin films and microchip technology [19-21]. These advanced developments in thin-film technology, micro-fabrication, and nano-fabrication have brought new insight into the use of liquid cells. The most commonly used support films during early days are 3 nm thick amorphous carbon films and graphene sheets [22-24]. But, but thin (20-100 nm) SiN films supported on silicon microchips are increasingly most popular and wildly used these days. This review focuses on the microchip-based liquid cell. These liquid cell microchips are typically only hundreds of nanometres thick, confined by two thin but robust electron-transparent membranes. The commercially available and by far most widely adopted liquid cell system is based on a silicon microchip.

At present, nanofluidic is entirely an imperceptive field and one needs new instruments, new mathematical algorithms, simulation, and techniques to observe what is going on in their distinctly different velocity-dependent nanofluidic regimes, for example, the study, presents a photon statistics method for quasi-one-dimensional sub-diffraction limited nanofluidic motions of single molecules using Feynman-Enderlin path integral approach which is validated in Monte Carlo simulation [25]. These results have not been theoretically as well as experimentally reported earlier. The results from this study are not restricted to a single-molecule environment of uniform electrodynamic interactions and can be used to investigate complex refractive index mismatch related to non-uniform single-molecule electrodynamic interactions as well. This study has the potential to define any kind of dynamics and transport problem where confinement and interactions are the major issues, the proposed theory can be used to understand what's exactly taking place and can give us absolute measurements such as electron or ion transport in 2D materials/nanowires and lipid bi-layers/cell membranes, sub-diffraction movement of planets or asteroids or clouds of dust or clouds in front of a star or multiple stars, human or animal movements in crowded train or supermarket or slums, currency exchange and flow, and molecular crowding/excitation-polarisation/quantum hydrodynamics [26-29]. The nanofluidic opening new avenues in the scientific world which is much needed now since the universe is fast-moving and the robustness with high throughput results is needed [1,25,30,31].

Discussion and Conclusion

These nanofluidic devices can bring new challenges as well as solutions in the field of nanoscience and engineering. Soon, we can see from recent devices trapping Nano scale object of less than 2 nanometre's in size, bio molecular interactions with DNA, protein aggregation, and cryoChip for high-resolution structural biology of molecules under physiological conditions can be also studied at the single-molecule level using a Shadow of an Electron Beam (SAEBD) based nanofluidic devices. Nanofluidic devices not only brings new technology to trap single molecules in fluid and also brings a lot of fundamental answers to nanotechnology,

but it also opens up the possibility of detecting early onsets of diseases. Single-molecule hand picking techniques at room temperature will be a paramount advancement of nanoscience and engineering, and we envision that there is a step towards that.

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