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Rapid concentration of deoxyribonucleic acid via Joule heating induced temperature gradient focusing in poly-dimethylsiloxane microfluidic channel

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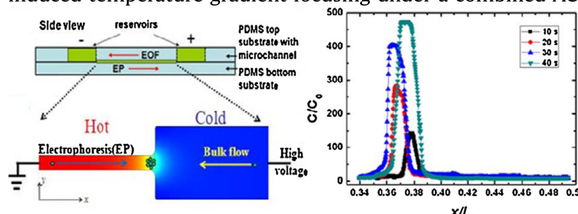
HIGHLIGHTS

- Rapid microfluidic concentration enhancement of DNA with 480 folds in 40 s.
- A new numerical model for Joule heating induced TGF by combined AC and DC field.
- First demonstration of DNA concentration enhancement using Joule heating induced TGF.

GRAPHICAL ABSTRACT

Rapid microfluidic concentration enhancement of deoxyribonucleic acid (DNA) with Joule heating induced temperature gradient focusing under a combined AC and DC electric field.



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ABSTRACT

This paper reports rapid microfluidic electrokinetic concentration of deoxyribonucleic acid (DNA) with the Joule heating induced temperature gradient focusing (TGF) by using our proposed combined AC and DC electric field technique. A peak of 480-fold concentration enhancement of DNA sample is achieved within 40 s in a simple poly-dimethylsiloxane (PDMS) microfluidic channel of a sudden expansion in cross-section. Compared to a sole DC field, the introduction of an AC field can reduce DC field induced back-pressure and produce sufficient Joule heating effects, resulting in higher concentration enhancement. Within such microfluidic channel structure, negative charged DNA analytes can be concentrated at a location where the DNA electrophoretic motion is balanced with the bulk flow driven by DC electroosmosis under an appropriate temperature gradient field. A numerical model accounting for a combined AC and DC field and back-pressure driven flow effects is developed to describe the complex Joule heating induced TGF processes. The experimental observation of DNA concentration phenomena can be explained by the numerical model.

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1. Introduction

The miniaturized medical/biomedical analysis systems can serve as promising platforms with high throughput, fast analysis, and good portability [1,2]. The increasing need of fast analysis and the decreasing amount of target analytes dictates that miniaturization to micro/nanoliter scale levels call for rapid and efficient preconcentration or focusing of dilute analyst/cell samples prior to analysis.

DNA detection has become one of the key technologies for various biomedical applications. Traditionally, PCR has to be used to amplify the amount of deoxyribonucleic acid (DNA) from the initial sample, before the use of a DNA detection technique. A variety of methods have been developed for pre-concentration of NDA molecules, allowing for PCR-free detection and analysis. Since most biomolecules are charged, electrokinetic-driven methods

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dominate in the field of preconcentration in micro/nanofluidic devices.

Electrokinetic trapping (EKT) method of DNA was reported by Dai et al. [3] who obtained concentration enhancement exceeding 100 folds via concentration polarization across an ion-selective membrane. Wang et al. [4] achieved million-fold concentration enhancement of DNA based on the EKT mechanism enabled by nanofluidic filters. However, the stability of EKT is dependent on various factors such as filter pore size, charge density of the nanostructure, and counteracting flow. The etched nano-channels can lead to incomplete charge exclusion and thus induce a counterflow which in turn would cause instability of EKT. Hahn et al. [5] proposed a field amplified EKT method to enhance the efficiency of EKT of DNA via a PET membrane. They also presented a theoretical model to identify the critical parameters of EKT. Liao and Chou [6] reported a new EKT method for rapid enrichment and mass transport of proteins based on electrodeless dielectrophoresis (DEP) using an array of insulating nano-constrictions as molecular traps, and they showed enhancement of proteins more than 10^5-fold in less than 20 s in high-conductivity physiological buffers. Kuo et al. [7] developed a micro-capillary electrophoresis chip for DNA preconcentration and separation using a normally closed valve which can be activated by pneumatic suction. The negatively charged DNA can be blocked and trapped by a nano-channel created by the normally closed valve. An approximate 41 times signal enhancement was obtained after 100 s of concentration time. However, the normally closed valve brings complexity in design and fabrication of microchips. Moreover, the requirement of precision nanomachining for fabricating nano channels/nanostructures hinders the wide use of nano-channel/membrane based EKT methods.

Various electrokinetic stacking and focusing methods have been developed for concentrating samples to a local equilibrium state. However, the field amplified sample stacking (FASS) [8] and the isotachophoresis (ITP) [9,10] usually need a relatively long channel to preconcentrate samples, which necessitates narrower structures to reduce band broadening. The sweeping method [11,12] works effectively only for small hydrophobic analytes with high affinity in a mobile micellar phase. Isoelectric focusing (IEF) [13] is restricted for analytes with an accessible isoelectric point. The electric field gradient focusing (EFGF) [14,15] involves complex designs and fabrications of multi-microelectrodes. Dghighi and Li [16] reported an electrokinetic method for concentrating DNA of about in a straight microchannel with two closed ends. A numerical study showed that the concentration process DNA transport can be simply controlled by manipulating the applied voltages via electrodes, and about 91 times concentration increase can be achieved within 115 s. Chen et al. [17] developed a capillary electrophoresis microdevice with a novel elongated double-T shape for DNA sample stacking used for multiplex mini Y short tandem repeat (STR) genotyping. Compared to conventional capillary electrophoresis microdevices with a cross-injection design, they showed that DNA samples can be preconcentrated in the stacking zone with 10 folds higher fluorescence peak intensities. In a subsequent work, Chen and Seo [18] demonstrated novel PCR-free variable number tandem repeat (VNTR) combined with the afore-mentioned elongated DNA sample stacking and capillary electrophoretic separation. They successfully identified the minisatellite tandem repeat number with only 5 fmol of DNA template in 30 min.

There are also some other focusing approaches using hydrodynamic flossing with flow control [19], AC electroosmosis (ACEO) [20–22] and thermophoresis [23]. Tresset et al. [19] proposed and demonstrated the use of microfluidic hydrodynamic flow focusing to achieve a fine control over the size of surfactant polyelectrolyte nanoparticles. Du et al. [20] designed an asymmetric quadrupole electrode platform to focus DNA based on combined ACEO, short-range dipole-induced self-attraction and AC DEP effects. They further demonstrated a head-on ACEO streaming capable of focusing and trapping DNA using double half-quadrupole electrodes in a symmetric arrangement [21]. However, the DNA concentration is only increased by a factor of about 10. Loucaides et al. [22] numerically analyzed DEP trapping of DNA with consideration of Steric effects and the effect of ACEO motion. Braun and Libchaber [23] proposed a method for trapping plasmid-sized DNA through interplay of laser heating induced thermophoresis and imposed hydrodynamic convection, and they showed more than one hundred of folds of DNA concentration enhancement within 180 s.

Temperature gradient focusing (TGF) is a field gradient focusing technique via balancing the electrophoretic motion of analytes against the bulk flow of buffer solution [24,25]. Ross's group proposed the TGF technique for a variety of analytes, including fluorescent dyes, DNAs, and proteins [24]. They further extended the TGF to two types of DNA hybridization assays [25]. Shameli et al. [26] reported a new bilinear temperature gradient method along the separation channel for improving both peak capacity and separation resolution simultaneously. However, the temperature gradient generated in these microdevices is through external heating/cooling sources. Instead of using external heating sources, Joule heating as a mean of generating temperature gradient has been studied for TGF of sample solutes [27–31]. This is because using Joule heating in TGF can consume less power, simplify the device construction and operation, and make the microdevice more portable without need of bulky external heating units. Realizing the negative backpressure induced flow effect with the use of sole DC field [27–30], we reported a novel Joule heating induced TGF technique utilizing a combined AC and DC electric field, under which about one order of magnitude higher concentration enhancement of fluorescein solutes was achieved [31]. In the present work, we demonstrate such combined AC and DC field induced Joule heating used for rapid TGF of DNA with concentration enhancement of 480 folds in a time duration of 40 s. Furthermore, we develop a numerical model to simulate such Joule heating induced TGF processes with our proposed combined AC and DC field technique. A thorough time scale analysis is conducted to simplify the governing equations. The numerical simulations with consideration of the back-pressure driven flow effect are compared with experimental results obtained in this work.

2. Theoretical formulation of Joule heating induced TGF under a combined AC and DC field

Fig. 1 illustrates the working principle of Joule heating induced TGF of DNA in a straight microchannel with sudden change in the cross-section. Fig. 1a shows such microfluidic device made from poly-dimethylsiloxane (PDMS) microchannel bonded with another PDMS sheet. With an electric field applied along the PDMS microchannel as shown in Fig. 1b, the motion of charged DNAs is resulted from two contributions: one is the bulk fluid velocity, u_{bluk}, arising from electroosmotic flow (EOF) from right to left since the PDMS microchannel usually obtains a negative surface charge in electrolyte, and the other is the electrophoretic velocity, u_{ep}, from left to right due to the electrophoresis for the negatively charged DNA. Usually, the total velocity of DNA analytes, $u_T = u_{\text{bluk}} + u_{\text{ep}}$ is not zero, and is proportional to the applied DC field strength. Once the strength of applied electric field is sufficiently high, a large temperature gradient is established across the sudden expansion conjunction section due to Joule heating effects [30,31] (Fig. 1c). Compared to u_{bluk},u_{ep} is more sensitive to temperature. Hence the total velocity, u_T can be manipulated through altering temperature profile along the channel axial

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