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研究課題名（和文）Development of Alternating Current Resistive Pulse Sensing Using Transport-Induced-Charge Theory

研究課題名（英文）Development of Alternating Current Resistive Pulse Sensing Using Transport-Induced-Charge Theory

研究代表者
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交付決定額（研究期間全体）：（直接経費）　　3,200,000円

研究成果の概要（和文）：ナノ細孔を有する薄膜を用いた粒子のセンシングが近年注目を集めている．直流電圧を用いたものが広く使われているが，電極での電気分解による電極の劣化やバブルの発生，溶液の pH の変化など継続的な利用を考えた場合多くの問題を抱えている．本研究は交流電圧を用いた電気浸透流ポンプの開発及び理論の解析を進めた．ジュール加熱の効果によって，輸送誘導電気浸透流（transport-induced-charge electroosmotic flow）の現象が向上することが示めされた．

研究成果の学術的意義や社会的意義
The Covid-19 pandemic has urgently increased the demand for high accuracy and throughout medical diagnostic methods. Our results have demonstrated that it is promising to control the flow within nanopore systems by thermal management for alternating current pumping and resistive pulse sensing.

研究成果の概要（英文）：Nanopore sensing has drawn attention in various fields, owing to its short processing time, ease of implementation, and ability to operate with limited sample volumes, paving the way toward high-precision medical diagnosis for various diseases. Albeit both direct current and alternating current systems have been used for electroosmotic pumping, direct current electroosmotic pumping suffers from notorious issues of bubble formation, electrode degradation, hydrodynamic instability, etc. originating from the redox reactions at electrodes. Thus, we develop alternative current electrokinetic pumping using transport-induced-charge (TIC) phenomena and investigate thermal effects in nanopore systems. Our results show that the rise of local temperature inside the nanopore significantly enhances TIC effects and thus has a significant influence on electroosmotic behavior. The results improve our knowledge of nonclassical electrokinetic phenomena for flow control in nanopore systems.

研究分野：Thermal Engineering

キーワード：Nanopore sensing　Nanofluidics　Electrokinetics　Electroosmosis　Joule heating

１．研究開始当初の背景

Water and charged particle transport through nanopores is pivotal in manifold nanofluidic applications including resistive pulse sensing, drug delivery, sea water desalination, nanofluidic battery and reverse electrodialysis. Albeit both direct current and alternating current systems have been used for electroosmotic pumping in nanopores, the direct current electroosmotic pumping could suffer from the notorious issues of bubble formation, electrode degradation, hydrodynamic instability, etc. originating from the redox reactions at the electrodes. These daunting problems stimulate the emergence of alternating current electroosmotic pumping as an appealing approach with potentially higher stability.

Nevertheless, current alternating current electroosmotic pumping scenarios based on dielectric patches or asymmetric nanopores cannot be applied to nanopore resistive pulse sensing. Not only does the integration of dielectric materials onto a nanopore require sophisticated fabrication techniques, but the interaction between the analytes and electrically polarized dielectric material will also significantly hinder the translocation events. Not to mention the current leakage through the dielectric material would be another formidable challenge. For asymmetric nanopores although they could facilitate recapture of molecules for investigating individual translocation events, the oscillating flow directions would lead to inaccurate results when estimating the analyte concentration. Confronting these obstacles, undoubtedly a new alternating current electroosmotic pumping strategy is needed to pave a way toward alternating current resistive pulse sensing for the next generation of diagnosis applications.

２．研究の目的

The objective of this project is to develop a novel alternating current nanopore pumping system for molecule sensing applications based on a transport-induced-charge (TIC) electrokinetic pumping system previously proposed [1]. It was shown that the reversal of the electric field simultaneously inverses the induced charge allowing the establishment of a unidirectional flow under the application of a periodic alternating current field. This unique phenomenon permits continuous water and nanoparticles pumping through an ultrathin nanopore in spite of the reversal of the electric field, implying that one can control alternating current electroosmotic flow via the manipulation of a salt concentration gradient across the nanopores for resistive pulse sensing.

３．研究の方法

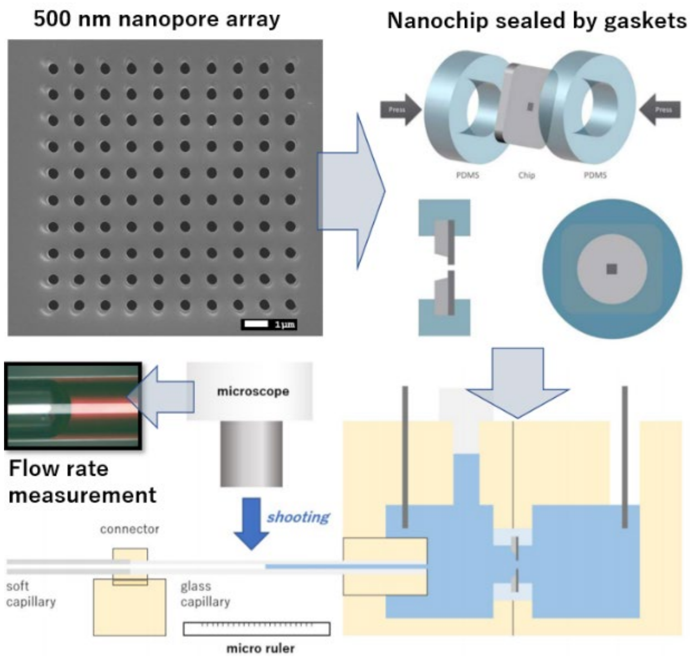

Figure 1. Experimental system for flow measurements.

As shown in Figure 1, in order to amplify the flow rate for electroosmosis measurements, we fabricated nanopore arrays on a thin membrane (50 nm in thickness) using focused ion beam etching. The chip was then fixed on a flow tank using polydimethylsiloxane (PDMS) gaskets. The flow tank was connected to a capillary tube, where the capillary force was balanced by an external pump until the liquid/air interface became stagnant. Once an external electric field was applied, the electroomotic velocity could be observed based on a volumetric method under a microscope.

The flow rate was compared with theoretical predictions and a computational simulation model was constructed to analyze thermal effects and flow behavior in the nanopores.

４．研究成果

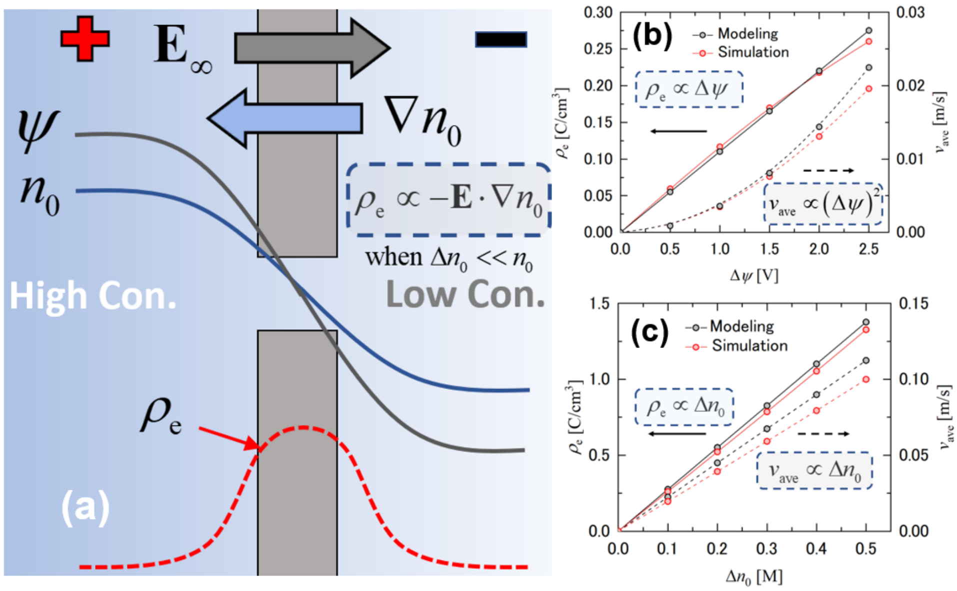

Figure 2. (a) Schematic of transport-induced-charge electrokinetic phenomena. ρ_e, $\mathbf{E}_\infty$, ψ and n_0 are the charge density, applied electric field, electric potential and solute concentration, respectively. Comparison between the analytical model and simulation results (b) at different imposed electric potential bias and (b) at different applied salt concentration different, where v_{ave} is the average flow velocity in the nanopore.

It is found that when a salt concentration gradient and an electric field are concurrently imposed across an ultrathin nanopore, the ionic concentrations of cations and anions become non-identical. This is attributed to the fact that the applied concentration gradient drives both ionic species toward the same direction (diffusing from the high concentration end to low concentration end) whereas the electric field forces the cations and anions to move in the opposite directions. As a result, the ionic concentration distributions become

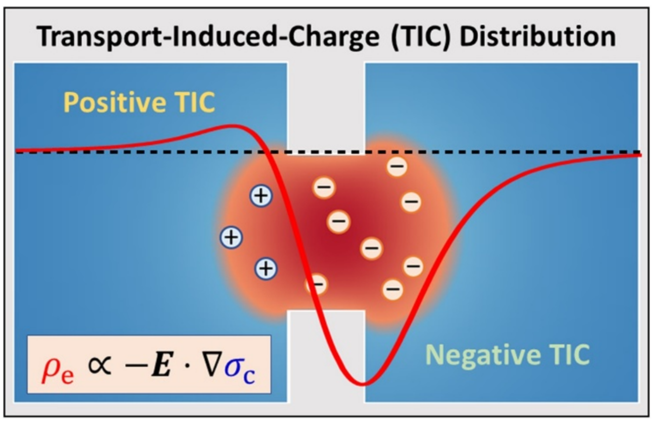

Figure 3. Schematic of transport induced charge distribution in a nanopore when thermal effects from Joule heating are considered.

different to satisfy the ions conservation. As a response to the electric force imposing onto the transport-induced-charge, the charged solution inside the nanopore is electroosmotically driven. We have constructed a simple analytical model to validate our simulation results as shown in Figure 2.

The develop a flow measurement system to detect electroosmotic flow in nanopores. While local flow behavior could not be directly observed, we theoretically investigated thermal effects due to Joule heating (JH) on TIC phenomena in an ultrathin nanopore (illustrated in Figure 3). Our results show that the rise of local temperature inside the nanopore significantly enhances TIC effects and thus elevating the electroosmotic velocity (v_z). As seen in Figure 4, the developed TIC electroosmotic flow (EOF) is in the opposite direction of electric double layer (EDL) electroosmotic flow in the vicinity of the surface. The Joule heating effects increase the magnitude of TIC EOF due to the decrease of local viscosity. These observations improve our knowledge of nonclassical electrokinetic phenomena for flow control in nanopore systems for the development of AC electrokinetic pumping.

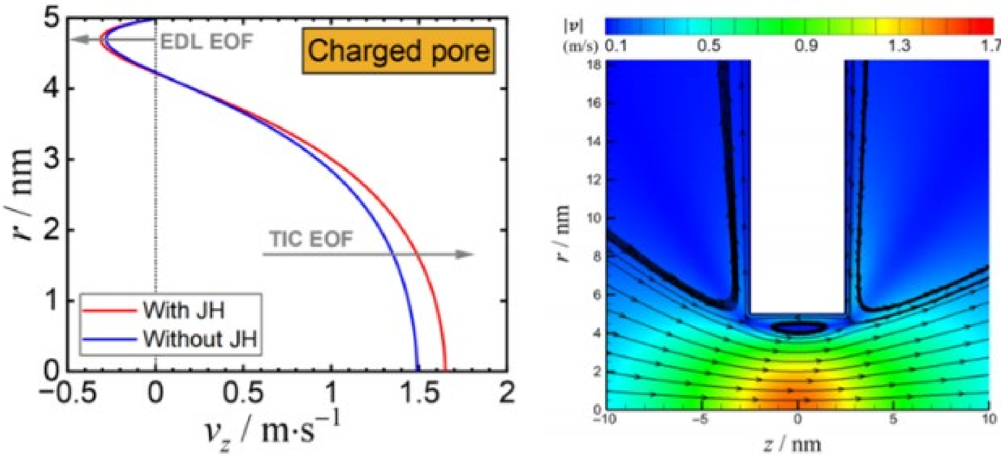

Figure 4. Transport-induced-charge flow profiles (*r,z*) in a negatively charged nanopore considering Joule heating effects. v_z stands for the flow velocity in the *z*-direction.

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[1] W.L. Hsu, J. Hwang, H. Daiguji *ACS sensors* **2018**, *3*, 2320-2326.

[2] Z. Wang, W.L. Hsu, S. Tsuchiya, S. Paul, A. Alizadeh, H. Daiguji *Micromachines* **2020**, *11*, 1041.

５．主な発表論文等

〔雑誌論文〕　計3件（うち査読付論文　3件／うち国際共著　2件／うちオープンアクセス　2件）

１．著者名 Zhixuan Wang, Wei-Lun Hsu, Shuntaro Tsuchiya, Soumyadeep Paul, Amer Alizadeh, Hirofumi Daiguji	４．巻 11
２．論文標題 Joule Heating Effects on Transport-Induced-Charge Phenomena in an Ultrathin Nanopore	５．発行年 2020年
３．雑誌名 Micromachines	６．最初と最後の頁 10411-104112
掲載論文のDOI（デジタルオブジェクト識別子） 10.3390/mi11121041	査読の有無 有
オープンアクセス オープンアクセスとしている（また、その予定である）	国際共著 －

１．著者名 Amer Alizadeh, Wei‐Lun Hsu, Moran Wang, Hirofumi Daiguji	４．巻 42
２．論文標題 Electroosmotic Flow: From Microfluidics to Nanofluidics	５．発行年 2021年
３．雑誌名 Electrophoresis	６．最初と最後の頁 834-868
掲載論文のDOI（デジタルオブジェクト識別子） 10.1002/elps.202000313	査読の有無 有
オープンアクセス オープンアクセスとしている（また、その予定である）	国際共著 該当する

１．著者名 Ru-Jia Yu, Su-Wen Xu, Soumyadeep Paul, Yi-Lun Ying, Ling-Fei Cui, Hirofumi Daiguji, Wei-Lun Hsu, Yi-Tao Long	４．巻 6
２．論文標題 Nanoconfined Electrochemical Sensing of Single Silver Nanoparticles with a Wireless Nanopore Electrode	５．発行年 2020年
３．雑誌名 ACS Sensors	６．最初と最後の頁 335-339
掲載論文のDOI（デジタルオブジェクト識別子） 10.1021/acssensors.0c02327	査読の有無 有
オープンアクセス オープンアクセスではない、又はオープンアクセスが困難	国際共著 該当する

〔学会発表〕　計4件（うち招待講演　0件／うち国際学会　3件）

１．発表者名 Wei-Lun Hsu and Hirofumi Daiguji
２．発表標題 Anomalous DNA Translocation Behavior through an Ultrathin Nanopore: Effects of Transport-Induced-Charge
３．学会等名 Royal Society of Chemistry (RSC) Tokyo International Conference 2019（国際学会）
４．発表年 2019年

１．発表者名 Wei-Lun Hsu, Yuji Nakagawa, Daisuke Egusa, Soumyadeep Paul, Ya-Lun Ho, Jean-Jacques Delaunay, Zhen Gu, Yi-Lun Ying, Yi-Tao Long, Eiji Abe, Yoshihiro Iwasa and Hirofumi Daiguji
２．発表標題 Two-Dimensional Nanopore DNA Sequencing by Diffusion Current Measurements
３．学会等名 2019 Materials Research Society (MRS) Fall Meeting（国際学会）
４．発表年 2019年

１．発表者名 Wei-Lun Hsu, Soumyadeep Paul, Zhen Gu, Ya-Lun Ho, Jean-Jacques Delaunay, Yi-Lun Ying, Yi-Tao Long and Hirofumi Daiguji
２．発表標題 Isothermal DNA Sensing Using Diffusion Current
３．学会等名 The 23rd International Conference on Miniaturized Systems for Chemistry and Life Sciences (MicroTAS 2019)（国際学会）
４．発表年 2019年

１．発表者名 Diffusiophoretic DNA Transport and Sensing in a Solid-State Nanopore
２．発表標題 Wei-Lun Hsu, Soumyadeep Paul, Ya-Lun Ho, Jean-Jacques Delaunay, Zhen Gu, Yi-Lun Ying, Yi-Tao Long, Hirofumi Daiguji
３．学会等名 第56回日本伝熱シンポジウムプログラム
４．発表年 2019年

〔図書〕　計0件

〔出願〕　計1件

産業財産権の名称	発明者	権利者
Analyzing Apparatus and Method Using A Pore Device	Wei-Lun Hsu and Hirofumi Daiguji	同左
産業財産権の種類、番号	**出願年**	**国内・外国の別**
特許、62853471	2019年	外国

〔取得〕　計0件

〔その他〕

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http://www.thml.t.u-tokyo.ac.jp/index.html

６．研究組織

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研究協力者	大宮司　啓文 (Daiguji Hirofumi)	東京大学・機械工学専攻・教授 (12601)	

７．科研費を使用して開催した国際研究集会

〔国際研究集会〕　計5件

国際研究集会	開催年
The 322nd Graduate Program for Mechanical Systems Innovation Seminar	2019年～2019年
The 321st Graduate Program for Mechanical Systems Innovation Seminar	2019年～2019年
The 319th Graduate Program for Mechanical Systems Innovation Seminar	2019年～2019年
The 302nd Graduate Program for Mechanical Systems Innovation Seminar	2019年～2019年
The 298th Graduate Program for Mechanical Systems Innovation Seminar	2019年～2019年

８．本研究に関連して実施した国際共同研究の実施状況

共同研究相手国	相手方研究機関