【Grant-in-Aid for Scientific Research (S)】

Broad Section D

Title of Project： Dynamic femtoliter reactor technology for next generation digital bioassays

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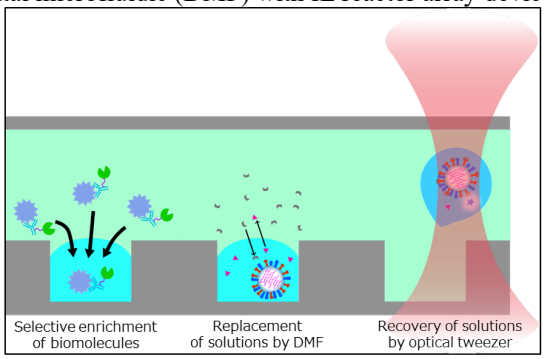
Keyword：Single molecule digital counting, Dynamic nano reactor technology

【Purpose and Background of the Research】

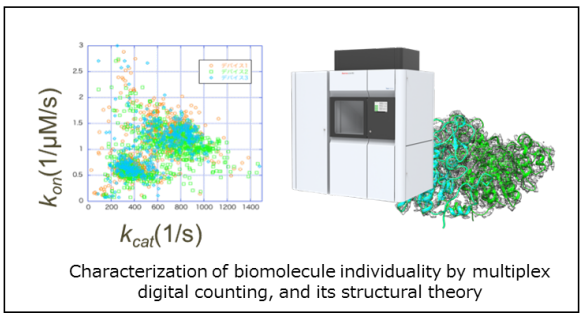
We have developed femtoliter reactor (fL reactor) array technology and lead the research of single molecule digital bioassays. However, conventional fL reactor arrays are not capable to actively condense and encapsulate target molecules, that is a bottleneck for further expansion of the research field and applications of digital bioassay. This project aims to develop new key technologies to confer "dynamic" functions on fL reactor array: active uptake and condensation of molecules, control of solution composition, and release of molecules from reactors or release of reactors themselves from array devices. Such technologies will enable the on-chip integration of conventional off-chip processes such as solutions exchange and sample condensation. These innovations will realize on-site single molecule digital diagnostics. These technologies will also pave a way for multidimensional digital bioassays that will reveal the molecular mechanisms of the polymorphism of activities of enzyme molecules and virus particles.

【Research Methods】

Firstly, we will develop"dynamic" fL reactor technologies which allow condensation of solutes, solution exchange, volume control, and release of solutes or reactors themselves. For this purposes, we will attempt to incorpotare unieque solution phenomena (eg, excluded volume effect) as well as dielectricphoresis (DEP) and digital microfluidic (DMF) with fL reactor array devices.



Next, based on this technological development, we will establish novel single molecule digital counting methods, and develop on-chip integrated digital bioassay technology (mainly ELISA). Moreover, we will develop multidimensional digital bioassay methods that quantitatively analyze the activity of individual molecules under various conditions in order to characterize their activity in multiple parameter space. These multidimensional digital bioassays will provide deep insights on how polymorphism among enzyme molecule or virus particles emerges.



Characterization of biomolecule individuality by multiplex digital counting, and its structural theory

【Expected Research Achievements and Scientific Significance】

Digital ELISA is regarded as one of the most promising bioassays for next generation clinical diagnosis. However, current system requires off-chip processes that hamper the realization of on-site high sensitive diagnostic tests. Once such off-chip processes are integrated on-chip digital ELISA, the total size of the assay system should be remarkably downsized, offering an avenue for on-site diagnosis that is indispensable for a personal medical care in future. In addition, this project will enhance our understanding on "molecular individuality", that will also bring important implications on how evolutional adaptation occurs at molecular level.

【Publications Relevant to the Project】

・Tabata KV, et al., Antibody-free digital influenza virus counting based on neuraminidase activity, *Sci Rep.* 31;9(1):1067 (2019)
・Zhang Y and Noji H, Digital Bioassays: Theory, Applications, and Perspectives, *Anal Chem.*, 89, 92-101 (2017)
・Rondelez Y, et al., Microfabricated arrays of femtoliter chambers allow single molecule enzymology, *Nature Biotechnology*, 23, 361-365 (2005)

【Term of Project】FY2019-2023

【Budget Allocation】138,800 Thousand Yen

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