Molecular mechanism of genome editing investigated by site-selective heat current analysis

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1．Project Purpose

It has been widely accepted that the thermal transport is one of the most fundamental biophysical properties of proteins. Nevertheless, its relationship with protein features, such as structure and dynamics, still remains elusive. We can expect highly non-uniform heat flow in proteins during thermal fluctuations because protein structures are anisotropic and inhomogeneous. To illustrate such nature of proteins, we developed a theoretical framework for analyzing local thermal transport property based on Green-Kubo formalism, constructed a linear-homopolymer-like model.

Intramolecular signaling, allosteric communication in proteins has been a long-standing issue in molecular biophysics. A variety of proteins systems, including genome editing proteins, have to do with this problem. We will address the issue based on the analysis of intramolecular vibrational energy relaxation network in proteins.

2．Results

We applied the linear-homopolymer-like model to a small α-helical protein, villin headpiece (HP36). As a result, it reproduced the exact value of the protein thermal conductivity, derived from the total heat current, with an error of less than 1 %. Interestingly, the site-selective analysis of the local, residue-wise, thermal conductivity demonstrated its distinct residue-type dependence, i.e., its magnitude decreased in the order of charged, polar, and hydrophobic residues. In addition, the local density of the residue-wise thermal transport property was also discussed.

3．Roles of the MCRP and its significance

To reproduce the thermal transport properties of complex macromolecules such as proteins based on Green-Kubo formalism, we need to perform careful MD simulation with a small timestep. As such, huge computational resources, i.e., CPU time and disc space, are required. We thank MCRP for providing us such computational resources to conduct our calculations during our scientific research

project.

4．Future plan

Regarding our future directions, we aim to understand (1) the mechanism of complex heat transfer mechanism within protein interior, (2) its relationship with the allosteric communication and signal transduction of proteins. Also, we wish to investigate the role of protein-solvent interface in the biophysical properties of proteins.

It is true that our own CURP program provides a unique method to analyze the thermal transport properties of proteins. From technical point of view, however, its computational efficiency is not sufficiently optimized for much larger protein systems. We wish to further improve the CURP program so that it demands less disc space with faster calculation speed.

5．Publications and conference presentations

(1) Journal papers

[1] T. Yamato, T. Wang, W. Sugiura, O. Laprévote, T. Katagiri, "Computational study on the thermal conductivity of a protein", *J. Phys. Chem. B.*, 126: 3029–36 (2022).

[2] T. Wang, T. Yamato, W. Sugiura, "Site-selective heat current analysis of α-helical protein with linear-homopolymer-like model", (under review)

(2) Presentations

[1] T. Yamato, "TBA", Telluride Science Research Center Workshop, Telluride, CO, USA, Jul. 24–8, (2023). (invited; vice-chair; co-organizer)

[2] T. Yamato, T. Wang, T. Katagiri, H. Morikawa, Y. Saito, W. Sugiura, Y. Arita, "タンパク質の部位選択的熱流解析法の開拓", 名古屋大学 HPC 計算科学連携研究プロジェクト、成果報告会, 名大, 2023 年 7 月 5 日

[3] T. Wang, T. Yamato, W. Sugiura, "Local thermal transport in an α-helical protein, 生物物理学会中部支部講演会, 名大, 2023 年 3 月 31 日

[4] T. Wang, T. Yamato, W. Sugiura, "タンパク質の局所熱輸送物性", 日本化学会春季年会, 東京理科大学, 2023 年 3 月 24 日

[5] T. Wang, A. Bonucci, V. Receveur-Bréchot, V. Belle, T. Yamato, "Structural and dynamical characterization of a highly flexible protein by AlphaFold-Multimer and MD simulations integrating DEER and SAXS data", 日本物理学会春季大会 (online), 2023 年 3 月 24 日

[6] T. Wang, T. Yamato, W. Sugiura, "Local thermal transport in an α-helical

protein", 物理学会春季大会(online), 2023 年 3 月 24 日

[7] T. Wang, T. Yamato, W. Sugiura, "Local thermal transport in an α-helical protein using EMD", 凝縮系の理論化学研究会, 沖縄, 2023 年 3 月 10 日

[8] T. Wang, T. Yamato, "Computational study on the signal transduction mechanism of dimeric sensor domain of FixL protein", 生物物理学会年会, 函館, 2022 年 9 月 29 日

[9] T. Wang, T. Yamato, "Computational study on ligands discrimination of dimeric sensory domain of BjFixL protein", 物理学会秋季大会,東工大, 2022 年 9 月 14 日

[10] 倭　剛久, "タンパク質のエネルギー流の理論計算", 学術変革領域(B)　低エネルギー操作　勉強会　講師, (online), 2022 年 9 月 2 日

(3) Others

[1] CURP (CURrent calculations for Proteins; https://curp.jp; https://github.com/yamatolab/current-calculations-for-proteins)

Supercomputer	Use	Allocated resources*	
		Initial resources	Additional resources
Cygnus	Yes	12545	
Wisteria/BDEC-01	Yes	190422	
*in units of node-hour product			