Local Thermal Conductivity: cross correlation

Abstract

This study aims to analysis the intra-residue heat conductivity and inter residue conductivity, determine the cross correlation coefficient.

1 Introduction

2 Materials and Methods

## 2.1 Thermal conductivity and Inter-atomic heat current

Based on linear response theory, the heat thermal conductivity in isotropic homogeneous systems can be expressed in terms of equilibrium time autocorrelation function of the heat current, ,

where is the thermal conductivity of a protein, is the volume of a protein, is Boltzmann constant, is the absoulute temperature of a sysetm, is the ensemble averaging term.[1](#ref-mcquarrie2000)

The instantaneous heat conductivity in a protein, , is given by[2](#ref-yamato2022)

where is the miscroscopic energy, is the position vector for each atom, and is the total number of atoms.

For the right hand side of the equation , it can be refered to two parts: “convective” term, , and “interaction” term, . It is widely accepted that “convective” term is the dominant term for gases and “interaction” term is the dominant term for solids, also applicable to biomolecular materials.[3](#ref-babaei2012)

In relatively rigid objects such as protein, the heat conductivity can be therefore be approximated as:

A general defination of the total energy of the sysetm, ,

where is the kinetic energy term, is the potential energy term position, is the momentum, = .

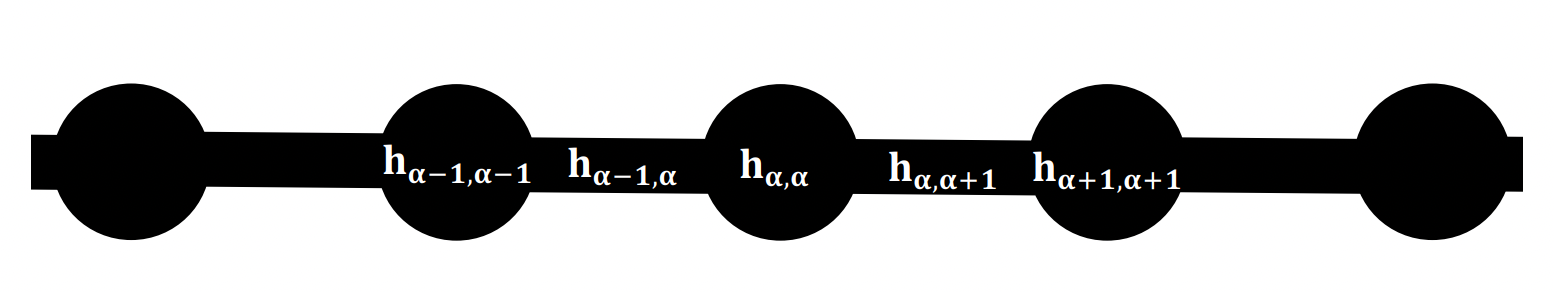
Then, the time derivative of for arbitrary atom can be expressed as

where is the force applied on atom from every other atom .

Then, heat conductivity in equation can be expressed as

Here, we define inter-atomic heat current between atoms and ,

## 2.2 Local Thermal Transport.



Model of linear homopolymer consisted of units of monomers (amino acid here). Each unit contains atoms.

The biomolecules is constrcted by connected amino acids with peptide bonds. In this study, we are considering the protein molecules as a linear homopolymer model and grouping the atoms in terms of amino acid residues. The dividing rule is shown in Figure . The total heat conductivity of a protein can be divided into two kinds of local heat conductivity: intra residue () and inter residue (). If we assume that the heat transport only occurs along the amino acid chain, then we can neglect the heat transport between residue pairs which are not adjacent.

Then, the total heat current can be expressed as,

where is the local heat current within number A residue (intra residue), , and atom and belong to residue ; is the local heat current between adjacent residues (inter residue), , and atom and belongs to residue and residue , respecitively and residue and are adjacent.

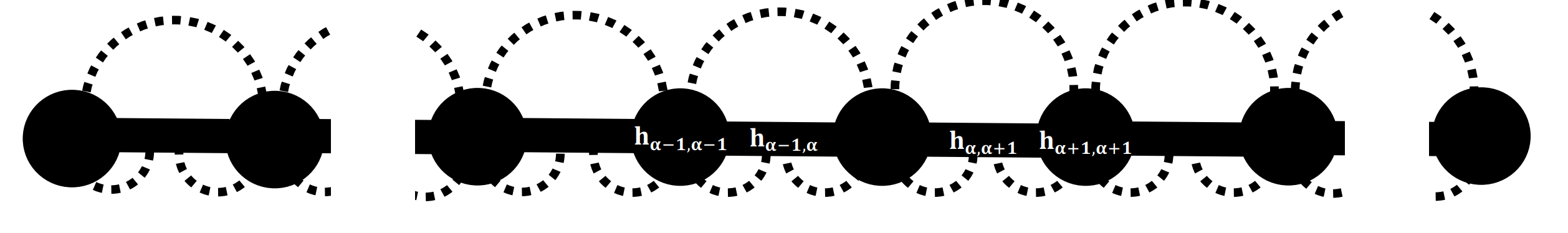
Likewise, base on equation , the local thermal conductivity of and , can be calculated by integrating the heat current autocorrelation function over time, Ideally, the summation of local heat conductivity of each piece should equal to the total heat conductivity.

where is the total heat conductivity, .

All heat currents and heat conductivity calculations are conducted by our CURP program[2](#ref-yamato2022),[4](#ref-takahisayamato2021) based on the trajectories of MD simulations.

## 2.3 Cross-correlation term calculation and local heat conductivity correction

Unfortunately, after preliminary calculation and analysis, equation does not hold, , see section [3.2](#X7ffd93865bc60f6431831db2605565dffbb7509). This may be because the cross-correlation effect among local heat currents from different parts.

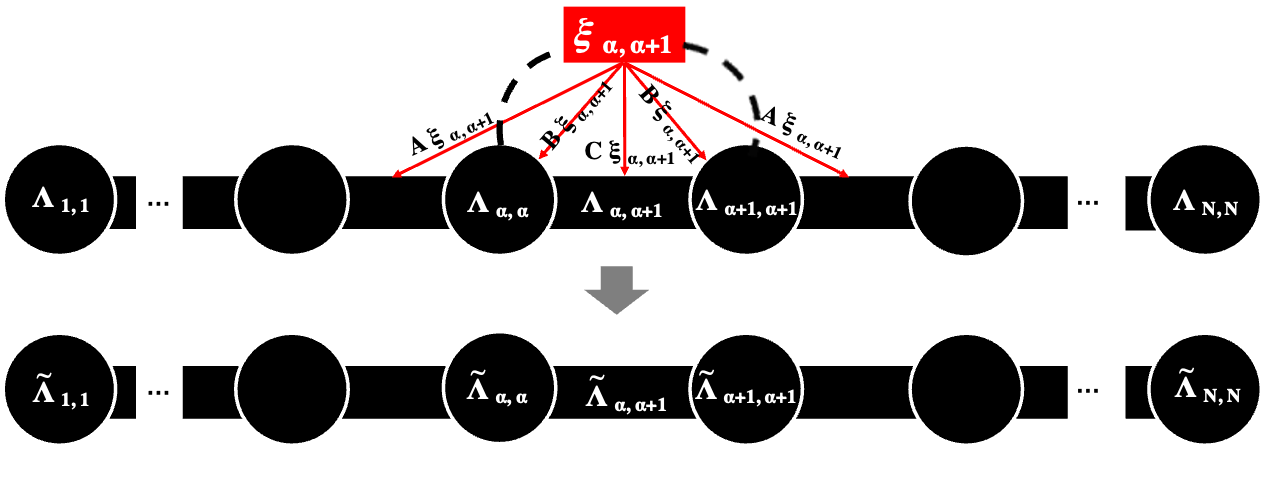


Assume that the cross correlation effect only happens between adjacent residues.

For correcting local heat conductivity, we introduced a cross-correlation term, . We assume that the cross correlation only occurs between adjacent local heat currents, as illustrated in Figure . We considered a dimer, which consisting of two adjacent residues numbered and . The local heat conductivity of dimer, , is expressed as

The cross-correlation of heat conductivity between two adjacent residues can be expressed as

We assume that the influence of cross-correlation term only ends within two postions starting from , shown in Figure , the contribution of , to and are considered as the same, marked as , to and are also considered as the same, marked as , and the contribution of to is marked as coeffient, after included the influence of cross-correlation in the local thermal conductivity, the local thermal conductivity within residue and those between residue can be expressed as



Allocation of cross-correlation term

According to Figure , and if we assume that the influence of on is greater than that of either of or , and let In the meantime, if we assume that the total weight of arbitrarily relevant in is equal to that in , then

combining equations , , and , , The quation and will become to , and .

## 2.4 Contribution of Partial Heat Current to the Overall Heat Current.

The contribution of partial heat current to the overall heat current can be evaluated by a contribution factor, , as follows:

We donated the contribution factor of intra-residue heat current to overall heat current as and of inter-residue heat current of adjacent residues as , respectively.

## 2.5 Equilibrium Molecular Dynamics Simulations

### *2.5.1 Simulation system building*

For the computation of the local thermal conductivity, the equilibrium molecular dynamics simulations are carried out with AMBER 19 package[5](#ref-d.a.case2019) based on the the nuclear magnetic resonace (NMR) crystal structure of villin headpiece protein, HP36 (PDB code: 1VII[6](#ref-mcknight1997)). The protein is immersed in a octahedral TIP3P model water solvent box of 2329 water molecules using LEaP program of AmberTools19. Amber ff19SB force field[7](#ref-tian2020) are used for protein HP36. All charged residues were considered in their standard protonation state at pH = 7.0. 4 chloride and 2 sodium ions are added to neutralize the simulation box and achieve a salt concentration of ~ 0.15 M. The periodic boundary condition was applied to the simulation system. Nonbonded particle-particle interactions[8](#ref-duan2001) are considered using a distance cutoff of 9 and the long-range electrostatic interactions are treated with the particle mesh Ewald (PME) method[9](#ref-salomon-ferrer2013).

### *2.5.2 Minimization and Equilibration*

Energy minimization of simulation system is conducted in three steps: (1) relaxation only on hydrogen atoms while the heavy atoms fixed, (2) relaxation on sidechain while the main chain atoms fixed, (3) relaxation on whole protein. Starting with the minimization conformation, 5 different Maxwell-Boltzmann velocity distributions at 0.1K are generated to perform equilibrium MD simulations which contains three steps: (1) heating system from 0.1 K to 300 K with positional restraints on the main chain atoms, (2) constant temperature, constant volume () ensemble MD simulation at 300K for 200 ps without positional restraints, (3) constant temperature, constant pressure () ensemble MD simulation at 300K for 700 ps.

### *2.5.3 Sampling MD simulations*

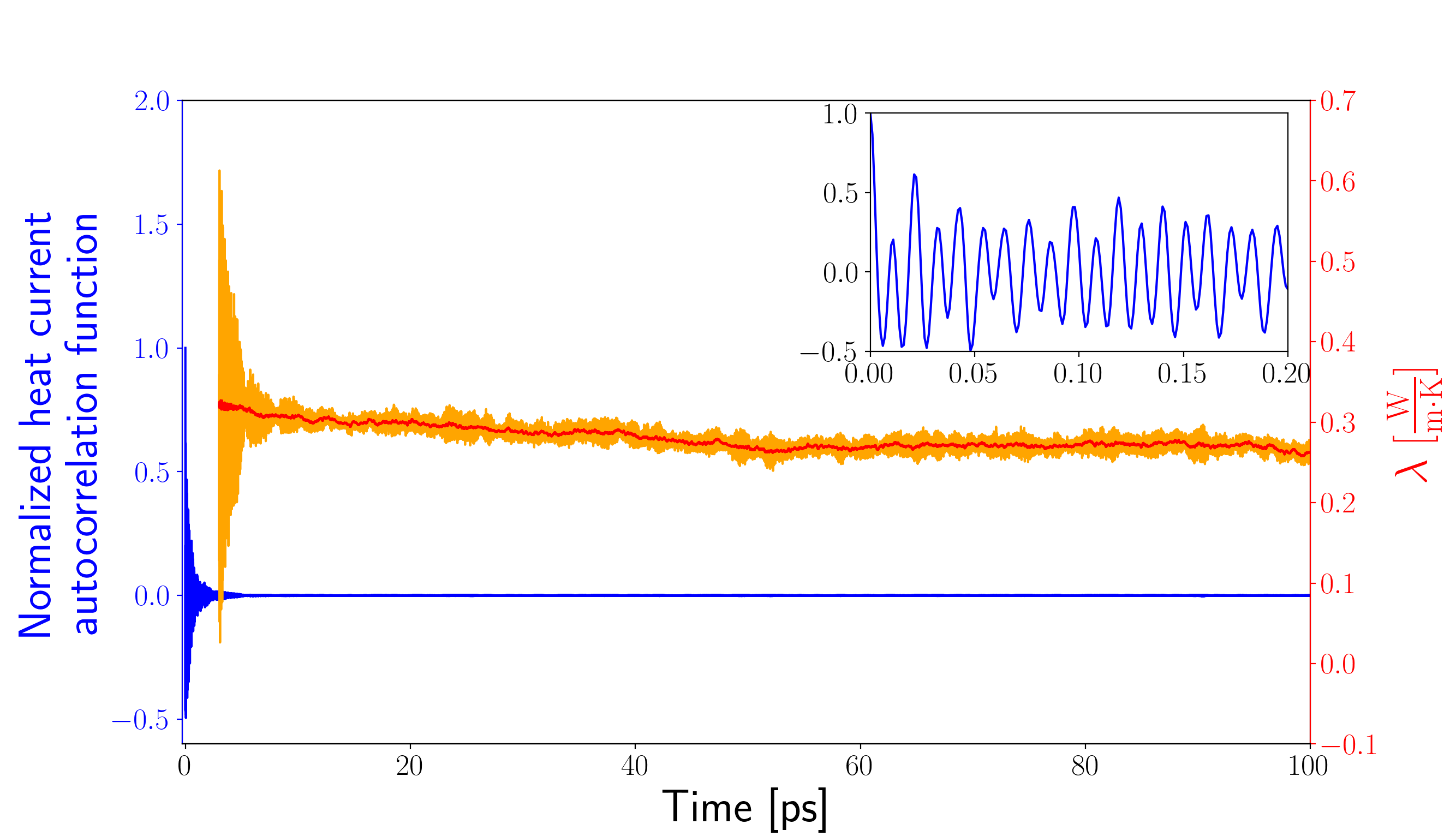
5 independent ensemble MD simulations, starting from the last frame of 5 MD simulation in equilibration, are performed for another 56 ns, which includes (1) 50 ns run with time a step of 2 fs, (SHAKE constraints is on for whole sysetm) (2) 1 ns run with time a step of 0.5 fs, (SHAKE constraint is off only for protein) (3) 5 ns run with time a step of 0.5 fs. (SHAKE constraint is off only for protein)

### *2.5.4 NVE MD simulations*

Snapshots with atomic coordinates and velocites are saved from every 500 ps in each of the last 5-ns sampling MD simualtions. With these snapshots, 50 sets of independent constant volumem, constant energy () ensemble MD simulations are conducted for 1ns with a time step of 0.5 fs and velocities were saved every 0.5 fs, while coordinates were saved every 1 fs.

3 Results and Discussion

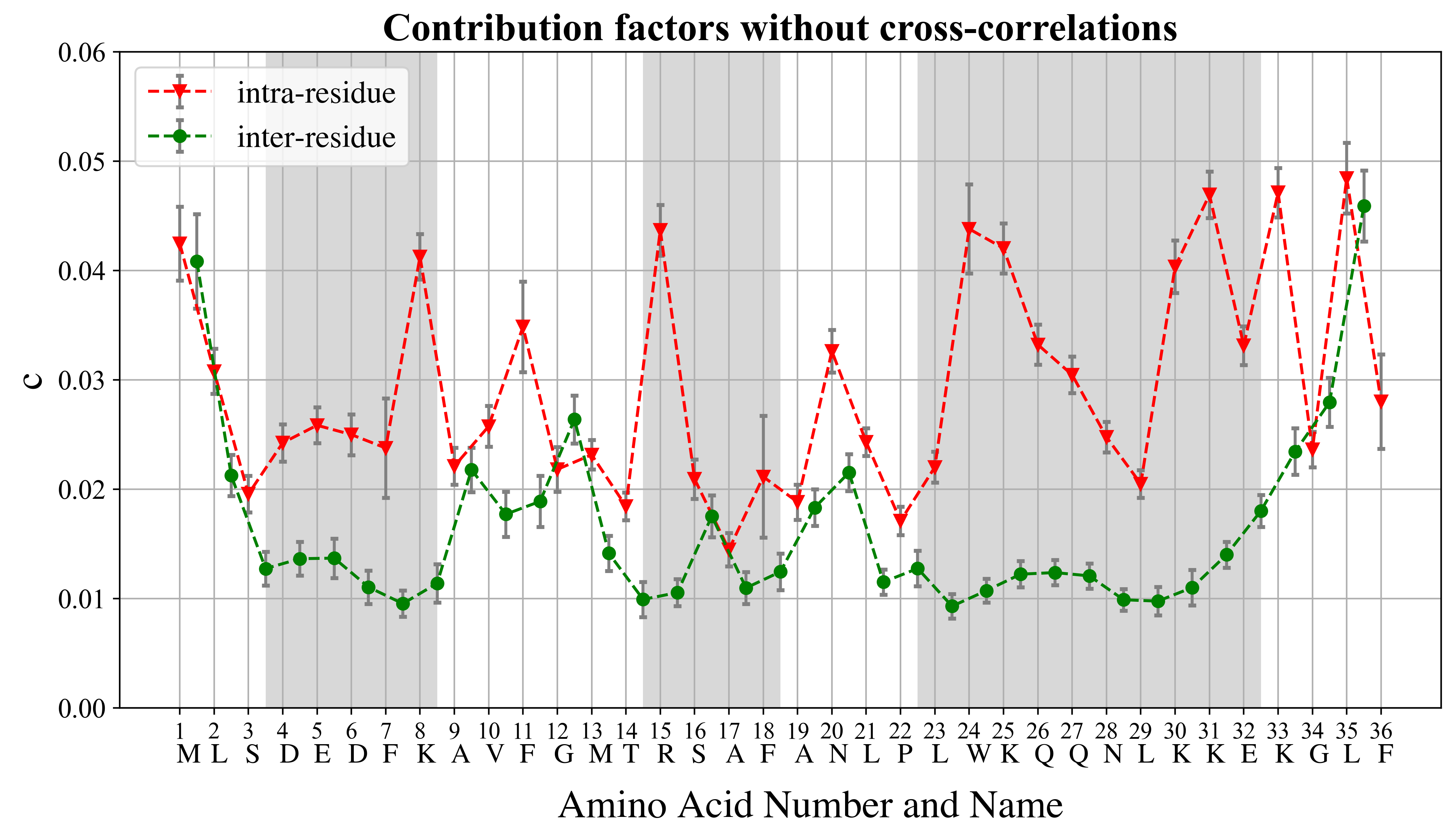
## 3.1 The overall thermal conductivity of HP36 protein.



Overall thermal conductivity of HP36 protein. Blue curve: The time evolution of ensemble averaged heat current autocorrelation function. The inset in blue is a drawing of partial enlargement of time 0-0.2ps. Yellow curve: The integral of heat current autocorrelation function with respect to time using trapezoidal rule. Red line: 100 fs running means.

The overall thermal conductivity, , of the HP36 protein was calculated based on equation . The volume of HP36 protein used in equation is 4845.447 $\AA^3$, same as the value in our previous paper[2](#ref-yamato2022) where the calcuation details can be found. The time evolution of ensemble averaged heat current autocorrelation function and value of are shown in Figure . Although the upper limit of integration time was set as 100ps, an integration time of 60 ps is long enough for to reach convergence with a regular fluctuations. was calculated as 0.26 0.01 with the integration time of 60 ps. In the followings, the integration time of 60 ps was used in the calculation of local thermal conductivity of HP36 when calculating contribution factors from of local heat current to the overal thermal conductivity.

## 3.2 Local heat conductivity

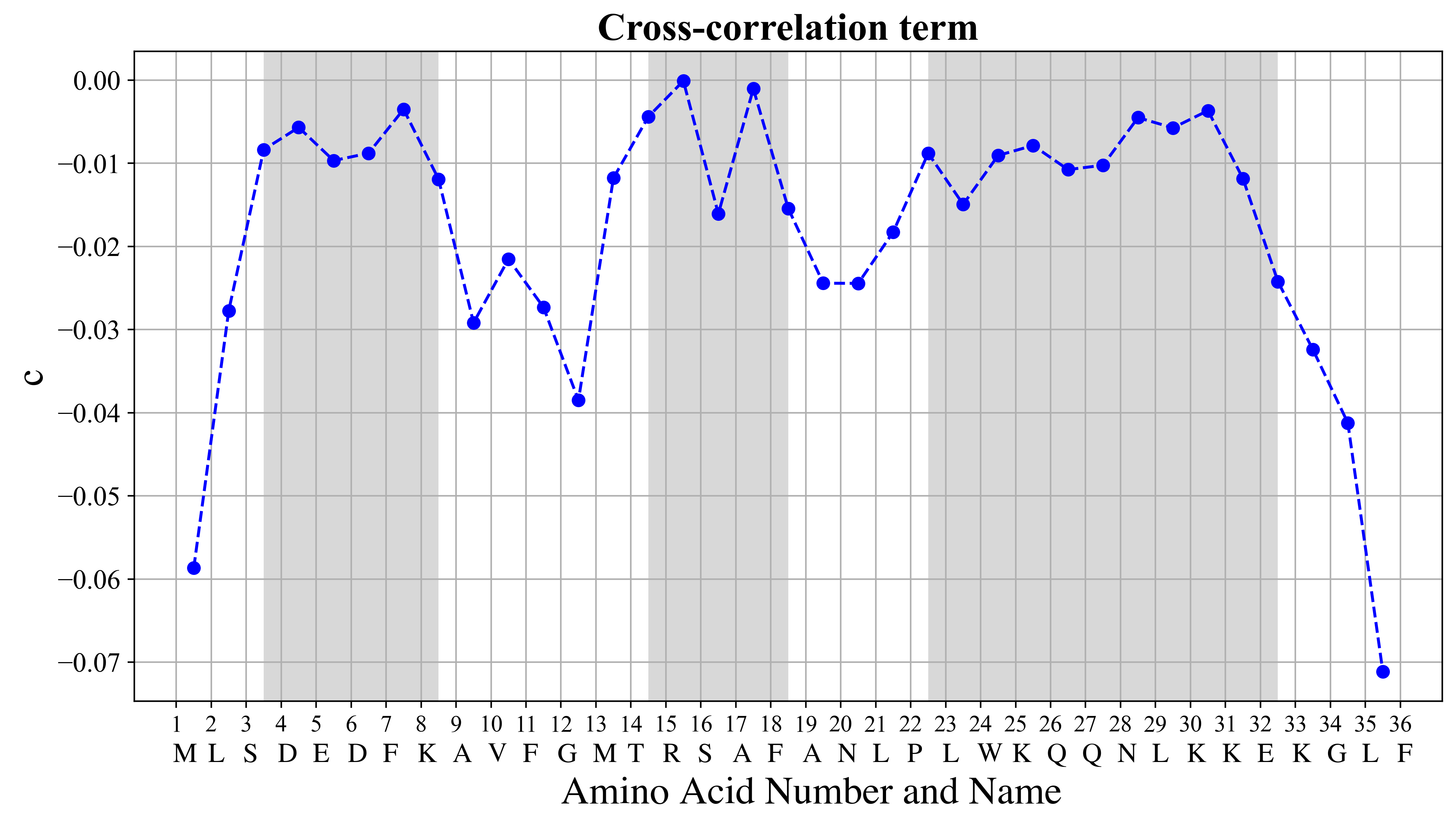


Contribution factors of intra-residue (, red) and inter-residue (, green) heat current to overall heat current in HP36 protein. The gray colored parts are residues in helices secondary structure.

The contribution factors of partial heat current of 36 intra-residue and 35 inter-residue heat current are plotted in Figure . Overall, the contribution factor of intra-residue is greater than that of inter-residue for two adjacent residue (, > , for example, , > ), expect for the residues in the termiuns of protein (Met1-Leu2, Leu35-Phn36) and Gly12-Met13. The averaged intra-residue heat conductivity, is 0.029, almost twice that of inter-residue, , which is 0.016, suggesting that the heat trasport within residue is the dominating way to contribute the overall heat current while the inter-residue heat current that through peptide covalent bonds is another dominating one compared with sidechain-sidechain way[2](#ref-yamato2022). The gray colored part in Figrue are residues of -helices in HP36 protein. Their local inter-residue heat conductivities () are all close to or lower than 0.15.

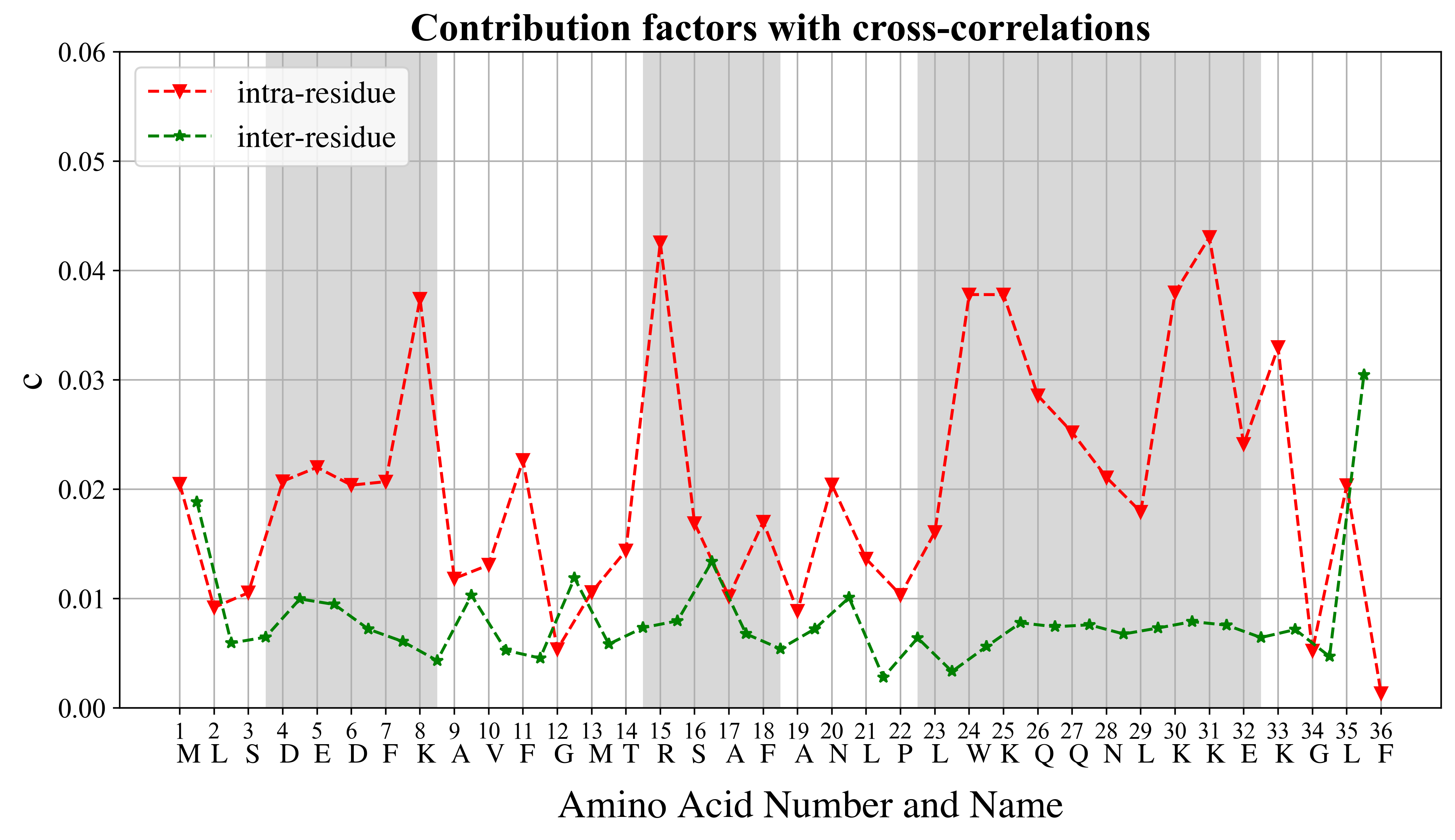
The summation of the intra-residue and inter-residue heat current contribution factors, are and , respectively. The total contribution factor of intra-residue and inter-residue heat current is not equal to 1 because of cross-correlations among different partial heat currents. So, in next section, we will examine the influence of the cross-correlation effect to the overall heat current.

## 3.3 Cross-correlation effect from adjacent residues



Cross-correlation term of local heat conductivity

Here, we consider the cross-correlation effect only happens between two adjacent residues. According to *Section* [2.3](#Xe0d88c5002b6cf7664052f1fc7d652cbdadccec), the cross-correlation term are calculated and plotted in Figure . The greater absolute value of , the stronger of cross correlation between two adjaect residues on heat transport. Except for the termius We can see that the absolute value of cross-correlation term in helices (gray background) are all close or lower than 0.1, suggesting the heat transfer between adjacent residues is less affected by each other.



heat conductivity after corrected

After allocation of cross-correlation term, the corrected local heat conductivities are plotted in Figure .

## 3.4 Comparsion between local heat conductivity and local heat diffusivity

## 3.5 Water model

In our previous study on thermal conductivity of protein[2](#ref-yamato2022), we used Amber ff14SB force-field + TIP3P water model with the SHAKE constraints switched off for MD simulations. It is known that the SAHKE restaints should be switched on for the rigid TIP3P water model. The remained question of water model effect on thermal conductivity calculation for proteins can be properly answered here. In this paper, we used Amber ff19SB + TIP3P water model with the SHAKE constraints switched off only for protein. According to equation , the thermal condctivity () of the whole protein is calculated as 0.26 0.01 , which is close to the value 0.3 0.01 in previous study[2](#ref-yamato2022).

4 Conclusions

Acknowledgements

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