

Binding of various amino acids or dipeptides derivatives of Schiff base copper(II) complexes to lysozyme

Takashi AKITSU^{1,*}

¹ Department of Chemistry, Faculty of Science,
Tokyo University of Science,
1-3 Kagurazaka, Shinjuku-ku, Tokyo 162-8601, Japan

We prepared single crystals of lysozyme binding Schiff base copper(II) complexes having various amino acids or dipeptides. Unfortunately, most of batch indicated dissociation of copper(II) ions. Only the crystallographic experiments using Ala and Gly-gly derivatives, the binding sites of metal complexes could be confirmed, though they differ from the expected features by spectroscopic experiments and computational results.

1 Introduction

It is known that the amino acid Schiff base copper complex not only exhibits SOD activity by itself, but also improves its activity when combined with egg white lysozyme [1,2]. Since the amino acid moiety of the ligand is expected to be involved in the reaction mechanism considered from computational chemistry, we aimed to try various amino acid derivatives and related ligands from both a computational and experimental standpoint.

2 Experiment

Using various amino acids or dipeptides, experiments were carried out according to the literature [1,2]. For example, salicylaldehyde and some *L*-amino acids were dissolved in methanol and stirred at 313 K for 1.5 hr to give a red solution. Copper(II) acetate-hydrate was added and stirred for 1 hr, and it was added and stirred for another hour to give a dark green solution. The reaction solution was allowed to stand at 298 K for 4 days to obtain green needle crystals. Commercially available lysozyme (Wako-Fujifirm) was used. After adjusting phosphate buffer solutions of copper(II) complexes and Lysozyme, we confirmed conventional spectra and grown the binding single crystals [2]. Data collection of X-ray diffraction was carried out at KEK-PF BL-5A as automatic measurement.

3 Results and Discussion

Docking calculations of lysozyme and copper(II) ions were performed using computational chemistry simulations with several softwares [3]. For example, it was revealed that Ala and His residues' scores were relatively high for binding site of copper(II) atom. The results were compared with experimental results of X-ray crystallography. Depending on the synthesis conditions, copper(II) ions dissociated and bonded in most cases, but a binding complex was barely observed for Ala (Fig. 1) and Gly-gly (Fig. 2) derivatives. However, it differs from spectroscopic experimental results [2], there are issues with reproducibility still at present.

References

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[2] D. Nakane, T. Akitsu *et al.*, *Frontiers in Chem.*, **11**, 1330833 (2024).

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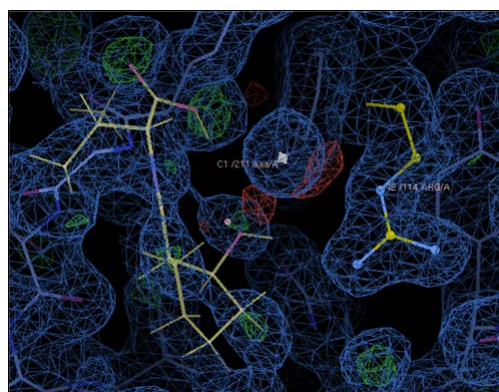


Fig. 1: Binding site of lysozyme and Ala-complex.

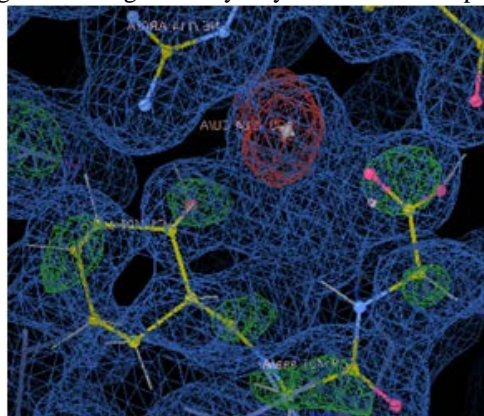


Fig. 2: Binding site of lysozyme and Gly-gly-complex.

Research Achievements

1. We obtained single crystals of lysozyme binding Schiff base copper(II) complexes having various amino acids or dipeptides.
2. According to X-ray crystallographic experiments of Ala- and Gly-gly- derivatives, the binding sites of metal complexes differs from the expected features by spectroscopic experiments and computation.

* akitsu2@rs.tus.ac.jp