MS09-P14

Allosteric coupling between autophosphorylation and phosphoryl-group transfer in a prototypical two-component signal transduction system

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Prototypical two-component signal transduction systems comprises a sensor histidine kinase (HK) receptor and a response regulator (RR). Input signals induce sensor HK autophosphorylation, and the subsequent transfer of the phosphoryl-group to the RR. Upon receiving the phosphoryl-group, the RR triggers an adaptive response, often at the transcriptional level. To gain insights into how the autokinase and phosphotransferase activities of the sensor HK are coordinated, we solved structures of the catalytic core domains of the prototypical CpxA-CpxR system [1]. Our data suggest a concerted switch -involving large-scale domain motions- by which autophosphorylation and phosphotransfer reactions are allosterically coupled.

References:

Mechaly, A.E., Soto Diaz, S., Sassoon, N., Buschiazzo, A., Betton, J.M., and Alzari, P.M. (2017). Structural Coupling between Autokinase and Phosphotransferase Reactions in a Bacterial Histidine Kinase. Structure 25, 939-944 e933.

Keywords: Histidine kinase, Response regulator, phosphotrasfer

MS09-P15

Helicobacter pylori urease structures by Cryo-EM and X-ray crystallography

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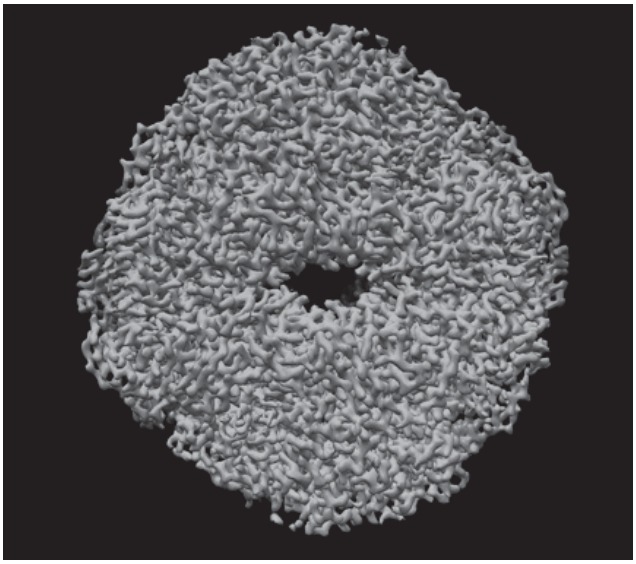
Half the world's population is chronically infected with *Helicobacter pylori*, causing gastritis, gastric ulcers and being the major risk factor for gastric adenocarcinoma. *H. pylori's* urease and proton-gated inner-membrane urea channel, *Hp*UreI, are essential for pathogen survival in the acidic environment of the stomach. The channel is closed at neutral pH and opens at acidic pH to allow the rapid access of urea to cytoplasmic urease. Urease produces NH_3 and CO_2, neutralizing entering protons and thus buffering the periplasm to a pH of roughly 6.1 even in gastric juice at a pH near 2. *The* urease crystal structures show a 1.1 MDa dodecameric assembly composed of two different subunits, α and β, 61.7 kDa and 26.5 kDa, respectively. The dodecamer is arranged in four copies of the trimeric $(\alpha,\beta)_3$ unit, resulting in a tetrahedral complex. Superposition of uninhibited and acetohydroxamic acid-inhibited crystal structures reveals a flap motion of a helix-turn-helix motif at residues α313–α346. When the inhibitor is bound, the flap moves outwards, creating an opening to the active site, whereas in the absence of the inhibitor the flap is closed, preventing access to the active site. The recent "resolution revolution" in cryoEM, driven by developments in instrumentation such as direct detectors, coupled with major improvements in data analysis, has put Cryo-EM at the forefront of structural biology for attaining high-resolution models in close-to-native conditions. Since 2015, several records have been achieved with the highest resolution structure reported so far for glutamate dehydrogenase (soluble protein, 1.8 Å), anthrax toxin (membrane protein, 2.9 Å) and hemoglobin (only 64 kDa, 3 Å). We have determined the structure of *H. pylori* urease using cryo-EM to a resolution of 3.1 Å and we compare it with the previously determined crystal structures.



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Keywords: Helicobacter pylori, Urease, Cryo-EM

MS10- Hydrogen-bonding & weak interactions studied by neutrons and X-rays

Chairs: Prof. Marta E. G. Mosquera, Dr. Matthew Blakeley

MS10-P01

Frequency and hydrogen bonding geometry of nucleobase homodimers in small molecule crystals

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The issue of various nucleobase pairs and their interactions occurring in RNA and DNA has been already studied from many different perspectives. In this survey, we wanted to approach the subject from more "chemical" point of view and see how nucleobases interact inside crystals. Our study is based on geometric data like bond lengths and bond angles taken from the Cambridge Structural Database (CSD), as well as types of protonation of investigated nucleobase, if the hydrogen positions were available.

We searched for nucleobase homodimers resembling those found in RNA and DNA, which means two nucleobases interacting through at least two hydrogen bonds formed in the molecule plane. The investigated compound were derivatives of adenine, guanine, hypoxanthine, thymine, uracil, and cytosine. We divided our findings into many categories including types of dimers, their protonation and if the N9 or N1 (for purines and pyrimidines respectively) is substituted with only hydrogen or larger substituent that may influence the way the nucleobase forms dimers. In our study, we analyze the various dependencies between the geometry of the molecule and what types of structures it prefers to form. We investigated not only neutral forms of nucleobases, but protonated too, and analyzed how protonation and charge influence the ability of a molecule to form homodimers.

Our study finds that for purines the most active edge is Hoogsten edge, taking part in the formation of dimers found in more than half of the investigated structures. Mixed interactions between the Hoogsteen edge and Watson-Crick edge are also very common, as they allow the molecules to align into infinite ribbons.

For pyrimidines, the situation is much different, as the various possible interactions between Watson-Crick edges of molecules dominate the charts. Only uracil behaves differently from thymine and cytosine, as it eagerly forms trans Watson-Crick - Hoogsten interaction, namely the Calcutta dimer. For all nucleobases, there is a common trend of sugar edge interactions being more frequent if the molecule is substituted with hydrogen in N9 or N1.