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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.

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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.