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Department of Chemistry

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Dynamics of ionic interactions involved in protein-DNA association

ABSTRACT: DNA recognition by proteins is highly dynamic. For example, transcription factors dynamically scan DNA through nonspecific interactions to locate particular DNA sequences. In the target DNA search process, the proteins change their location on DNA from one site to another not only through dissociation and reassociation, but also through sliding and intersegment transfer. Protein-DNA interactions involve dynamics of ions as well. Counterions condensed around DNA are released upon protein's binding to DNA. Intermolecular ion pairs between protein side-chain and DNA phosphate groups undergo dynamic transitions between the contact ion-pair state and the solvent-separated ion-pair state. Using nuclear magnetic resonance (NMR) methods, we study these dynamics involved in the protein-DNA interactions. In this presentation, our recent studies on the ion dynamics in the protein-DNA association process will be introduced.

BIO: I have been studying biophysical chemistry of protein-DNA interactions throughout my entire career. In my Ph.D. work at University of Tokyo, I learned nuclear magnetic resonance (NMR) and fluorescence spectroscopy and studied protein-DNA interactions involving human centromere proteins in collaboration with Prof. Okazaki. In my postdoctoral trainings at Prof. Robert Clubb's laboratory (UCLA) and at Dr. Marius Clore's laboratory (NIH), I learned NMR spectroscopy and developed some unique NMR methods for investigating dynamics of protein-DNA interactions. These methods are powerful for studying the dynamic processes whereby proteins scan and recognize DNA. Since I became independent in 2007, I have successfully administered 4 NIH-funded projects, 3 NSF-funded projects, and 3 private foundation projects as the PI for our research on protein-DNA interactions. For a more comprehensive understanding of protein-DNA dynamics, my research group routinely uses NMR spectroscopy as the primary means and also applies various other biophysical and biochemical approaches, including stopped-flow fluorescence spectroscopy, Isothermal titration calorimetry (ITC), X-ray crystallogphy, and small-angle X-ray scattering. My current research focuses on the dynamic processes whereby transcription factors scan DNA and recognize their target sites.

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2. Anderson KM, Esadze A, Manoharan M, Brüschweiler R, Gorenstein DG, Iwahara J. (2013) Direct observation of the ion-pair dynamics at a protein-DNA interface by NMR spectroscopy. J Am Chem Soc 135, 3613-9.
3. Esadze A, Kemme CA, Kolomeisky AB, Iwahara J. (2014) Positive and negative impacts of nonspecific sites during target location by a sequence-specific DNA-binding protein: origin of the optimal search at physiological ionic strength. Nucleic Acids Res 42, 7039-46.
4. Zandarashvili L, Esadze A, Vuzman D, Kemme CA, Levy Y, Iwahara J. (2015) Balancing between affinity and speed in target DNA search by zinc-finger proteins via modulation of dynamic conformational ensemble. Proc Natl Acad Sci U S A 112, E5142-9.