蔡旻燁論文列JACS 國際跨校學術合作成果亮眼

學校要聞

【記者劉江淡水校園報導】化學系助理教授蔡旻燁以第一作者身分在美國化學學會出版的《Journal of the American Chemical Society》（簡稱為JACS）期刊發表論文「Multiple Binding Configurations of Fis Protein Pairs on DNA: Facilitated Dissociation versus Cooperative Dissociation」（成對的Fis蛋白質在DNA上的多種結合組態：促進解離與合作解離）。

該期刊是化學領域中的頂尖期刊，也是科技部自然司化學學門列名的「指標性期刊」，為SCI所收錄，2018年影響因子更高達14.695，在同類期刊中排名前25%（12/172 ＜ 7%）。該篇論文以「基因調控的分子機制」為研究主題，透過理論計算方法，模擬蛋白質與基因（DNA）交互作用的動態過程，發現蛋白質從DNA分離的兩種途徑：促進解離和合作解離。前者的生物意義在於有助於細胞內的核相關蛋白質「汰舊換新」，後者可作為基因表達的「分子開關」。該研究預測的蛋白質—DNA的協同組裝、構型以及控制途徑，為細胞內基因調控機制的新原型，挑戰當前系統生物學方法所使用的標準模型！

蔡旻燁表示：這項工作透過與美國萊斯大學理論生物物理中心的研究團隊合作，成功將國外知名大學的計算資源、分析方法引進淡江，建立在化學系所挹注的高速計算設備。此舉預計能夠帶動實驗室專題生以及研究生的參與。在此基礎之上，我們打算開發雲端計算資源，並將實驗室的研究方向延伸至人工智慧（AI）相關的生化應用課題，與國際接軌，從而在「計算生物物理」領域的基礎研究上佔有一席之地！

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Multiple Binding Configurations of Fis Protein Pairs on DNA: Facilitated Dissociation versus Cooperative Dissociation

Min-Yeh Tsai,[†,§,∥] Weihua Zheng,[†,§] Mingchen Chen,[‡,§] and Peter G. Wolynes*[,†,§]

[†]Department of Chemistry, [‡]Department of Bioengineering, and [§]Center for Theoretical Biological Physics, Rice University, Houston, Texas 77005, United States

[∥]Department of Chemistry, Tamkang University, New Taipei City 25137, Taiwan (R.O.C.)

Supporting Information

ABSTRACT: As a master transcription regulator, the Fis protein influences over two hundred genes of *E. coli*. The Fis protein's nonspecific binding to DNA is widely acknowledged, and its kinetics of dissociation from DNA is strongly influenced by its surroundings: the dissociation rate increases as the concentration of the Fis protein in the solution phase increases. In this study, we use computational methods to explore the global binding energy landscape of the Fis1:Fis2:DNA ternary complex. The complex contains a binary−Fis molecular dyad whose formation relies on complex structural rearrangements. The simulations allow us to distinguish several different pathways for the dissociation of the protein from DNA with different functional outcomes and involving different protein stoichiometries: (1) simple exchange of proteins and (2) cooperative unbinding of two Fis proteins to yield bare DNA. In the case of exchange, the protein on the DNA is replaced by the solution-phase protein through competition for DNA binding sites. This process seen in fluorescence imaging experiments has been called facilitated dissociation. In the latter case of cooperative unbinding of pairs, two neighboring Fis proteins on DNA form a unique binary−Fis configuration via protein−protein interactions, which in turn leads to the codissociation of both molecules simultaneously, a process akin to the "molecular stripping" seen in the NFκB/IκB genetic broadcasting system. This simulation shows that the existence of multiple binding configurations of transcription factors can have a significant impact on the kinetics and outcome of transcription factor dissociation from DNA, with important implications for the systems biology of gene regulation by Fis.