2SD04

Intrinsic Disorder and Protein Function

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Many proteins fail to fold into unique 3-D structures, existing instead as conformational ensembles. The amino acid composition of a disordered collection differs markedly from that of an ordered collection: the compositional differences between ordered and disordered proteins have been used to construct several different predictors of natural disordered regions (PONDR[®]s). Application of the various PONDR[®]s to whole proteomes indicates that intrinsic disorder is unexpectedly common, especially in eukaryotic cells. Much of this disorder is involved in signaling and regulation. For example, phosphorylation sites are commonly located in regions of disorder. Many disordered regions have localized partner-binding regions that we are calling molecular recognition elements or MoREs. All together these data and observations suggest two parallel paradigms for protein structure-function. The classical paradigm of *sequence to 3-D structure to function* holds for enzymes. Catalysis requires a pre-organized active site, which in turn requires a stably folded protein. The new view of *sequence to disordered ensemble to function* holds for signaling and regulatory proteins and regions. Disorder to order upon binding has advantages for signaling and regulation, for example in the facilitation of high specificity coupled with low affinity to enable binding reversibility and in the facilitation of binding diversity to enable multiple partnerships and complex signaling networks with hubs.

K.A.Dunker : Intrinsic Disorder and Protein Function

2SD06

Computational design of water-soluble analogues of the potassium channel KcsA

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Membrane proteins and water-soluble proteins differ largely by their exposed residues. Given the similarities of their buried cores, we have demonstrated that a membrane protein can be made water-soluble by mutating exposed residues to water-soluble ones, while retaining much of the structure and properties of the parent protein. We took a computational approach to water-solubilize the tetrameric bacterial potassium channel KcsA, for which the three-dimensional structure is known to high resolution. The generated water-soluble potassium channel analogues, WSK-1, -2, and -3 have been confirmed that they exist largely in a monomer-tetramer equilibrium and possess the same amount of alpha-helical secondary structure as KcsA. WSKs also bind specifically to the K⁺-channel toxin Agitoxin2 with a 1:1 tetramer:toxin ratio, as well as the salt tetraethylammonium, as has been observed for toxin-binding mutants of KcsA. In the symposium, we show how our computational design works for the protein solubilization.

H.Kono, A.M.Solvic, J.D.Lear, J.G.Saven and W.F.DeGrado : Computational design of water-soluble analogues of the potassium channel KcsA

2SD05

Protein structure predictions for new fold targets in CASP6

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One of the challenges of the post-genomic era is to assign three-dimensional structures computationally to proteins encoded in genome sequences. To understand the capabilities and limitations of current prediction methods, CASP (Critical Assessment of Techniques for Protein Structure Prediction) experiments have been held every two years since 1994. The most recent CASP was CASP6 in summer 2004. In this presentation, we describe how we did and what we have learned from CASP6, focusing on the sub-area of new fold (NF) prediction.

For CASP6, we use SimFold, a protein simulation program that we have been developed. SimFold uses a coarse-grained protein model that has explicit backbone atoms and a sphere at the center of mass of sidechain. The energy function is based on physico-chemical consideration and consists of many terms such as hydrophobic interaction, hydrogen bonds, and so on. For conformational sampling, SimFold uses the fragment assembly (FA) method. Our FA is different from what has been developed by Baker's group. Typical FA protocol does not obey the detailed balance, but our algorithm does. Thanks to this property, we could even combine the FA with the multicanonical ensemble approach which is indeed used in CASP6 and helps conformational sampling very significantly. Structures at the center of large clusters are chosen as predicted models.

G.Chikenji, Y.Fujitsuka, S.J.Park and S.Takada : Protein structure predictions for new fold targets in CASP6

3SA01

Web services が加速するバイオ情報環境

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インターネットと World Wide Web の普及によって、分散しているデータベースやデータ解析プログラムを利用できるようになった。たとえば、論文データベースから抽出した論文にあるアクセション番号を使って、国際塩基配列データベースから該当する配列データを取り出し、手元の配列データと組み合わせた多重整列をし、進化系統樹を描くことができる。

しかし、これまではこうした検索と解析の手順（ワークフロー）を実行するには、あるサイトに接続して結果を受け取り、その結果を次のサイトの入力としてコピーするという手作業を繰り返す必要があった。あるいは、各サイトの仕様を自ら解析して利用者がプログラムを開発する必要があった。

これまでの Web サイトは Web ブラウザーを介して、人間にとってそれ以前とは比べ物にならないほど使いやすい情報環境を提供してきた。これからは、情報資源が大量になりかつ処理するデータが大量になってきたため、人間が直接操作するよりも、コンピュータプログラムから操作しやすい Web サイトも必要になっていく。Web services はまさに、このコンピュータプログラムが扱いやすいインターフェースを提供する技術である。

Web services の世界では、コンピュータプログラムが、多様な Web services の登録ディレクトリーに問い合わせ、コンピュータプログラムが必要なサイトとそのサイトの利用のための仕様を獲得し、コンピュータプログラムがそのサイトに直接処理を依頼し、そこから受け取った結果を手元のデータベースに格納できるようになる。日本 DNA データバンク (DDBJ) では公共データベースとして、国際的にも早い時期から Web services を提供してきている。本講演ではこの経験を中心にバイオ分野における Web services の広がりを紹介する。

H. Sugawara : Web services will expand the rich information environment for biology