2SC06

Recovery of Photoreceptor Responsiveness Following Intense Bleaching Exposures

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Following exposure of our eye to intense illumination that “bleaches” a substantial fraction of visual pigment, the sensitivity of our overall visual system is initially greatly depressed, and recovers only slowly with the progression of time. In a number of ways this desensitization is indistinguishable from the effects of a background light, and hence the recovery of sensitivity during dark adaptation resembles the fading of an “equivalent background intensity”. The equivalent light originates in the photoreceptors, and can be monitored in the living human eye by measuring the electroretinogram (ERG) response to flashes of light.

In the rod system, bright flashes can be used, to obtain a measure of the circulating rod current. The size of this circulating current at first falls to a low level after a large bleach, but then recovers with time in the dark. The kinetics of recovery show a close parallel to the recovery of overall visual sensitivity, and in both cases it is possible to extract the time-course of pigment regeneration.

In the cone system, the response to a dim test flash can provide a measure of sensitivity, and thereby an estimate of the level of visual pigment. For both the rod and cone systems, the speed of regeneration of visual pigment appears to be limited by the rate at which new chromophore, 11 cis retinal, is able to move from a pool (e.g. in the retinal pigment epithelium) to the location of bleached opsin in the photoreceptor outer segment.

T.D. Lamb : Recovery of Photoreceptor Responsiveness Following Intense Bleaching Exposures

2SD02

Protein folds and knots

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Protein folds are considered as simple directed chains. Local smoothing of their coordinate sets (without chain passage) leads to a simple method to detect knots in open chains. Atrefoil and figure-of-eight protein knot are described. Extension of the algorithm to incorporate hydrogen-bond cross-links allows protein pseudo-knots to be considered. The general connectivity of a protein chain is considered as a graph and a novel concept of topological accessibility described. These ideas are then applied to semi-random folds.

W. R. Taylor : Protein folds and knots

2SD01

最新の新規フォールド検出のためのPDB alert システム

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タンパク質ドメインの立体構造を分類すると多くのドメインが同じフォールドをとる(2次構造要素の空間配置が同じ)ことが分かる。この現象は配列間に統計的に有意な類似性がない場合でも起こる。このように配列の異なるドメインでも同じフォールドが繰り返し現れるので、配列の多様さに対してタンパク質ドメインのとりうるフォールドの数は限定されたものになることが示唆される。実際、タンパク質ドメインの立体構造を分類したデータベースであるSCOPの最新版によればPDBに登録された20619個のタンパク質(2003年8月1日のデータ)は高々800のフォールドに分類される。この数はChothiaによって推定されたタンパク質ドメインがとるであろうフォールド数である1000という数字に迫っている。では、もうタンパク質がとるフォールドはほぼ全て出そろったのだろうか?あるいは、これまでのフォールドにない新規のフォールドが次々解かれているのだろうか?また、それはどのようなフォールドなのだろうか?このような最新の新規フォールドに対する問いに答えるために我々はPDB alert システムを構築した。PDB alert システムはPDBの更新にあわせて自動的に新規フォールドの候補を提示する。PDBには毎週100程度の構造が新規に登録されており、これらを既存のフォールドと比較することで新規フォールドの候補を絞り込む。このさい、既存の配列比較法や構造比較法を組み合わせることで自動化を実現している。当日はPDB alert システムと最新の新規フォールドについて詳しく説明する。

R. Koike, K. Kinoshita, K. Yura and M. Ota : PDB alert system for finding the latest New Fold

2SD03

Multiple associations of DNA strands with non-complementary sequences and their biological implications

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The DNA double helix, proposed by Watson and Crick 50 years ago, is composed of the two strands aligned in an anti-parallel fashion and associated to each other through hydrogen bonds formed between the complementary bases (A and T) and (G and C). Since the life was evolved based on this system, it is difficult to find different structures in the stationary state. However, it is not the case when DNA takes a single-stranded state in dynamical events, such as replication, transcription, and recombination, and so on. We solved several crystal structures of DNA fragments with the sequence d(GCGAXAGC) (X=A,G,T,C) and the related mutants, and found that these fragments form a base-intercalated duplex different from the well known base-paired duplex.

Recent interests are shifting to functions and structures of repetitive sequences found in non-coding regions on genome, which are related to some genetic diseases. In a crystal of the fragments with d(gcGA[G]_nAgc) n=1, obtained at low K⁺ concentration, four base-intercalated duplexes are assembled to form an octaplex, so that the eight G₅ residues form a stacked double G-quartet in the central part. While, in the crystal obtained at slightly high K⁺ concentration, the octaplex is split into just two halves. These structural features suggest a folding process of eight repeats found in the human VNTR, according to a double Greek-key motif. Such a packaging of the repeats will facilitate slippage of a certain sequence during replication, to induce increase or decrease of the repeats.

A. Takenaka : Multiple associations of DNA strands with non-complementary sequences and their biological implications