PLENARY LECTURES

PL1

Molecular Principles of Protein Structure and Protein-Protein Interaction

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The genesis of the now known Ramachandran map will be briefly outlined. The signifance of the phi-psi map and the underlying molecular principles of protein conformation will be highlighted. A model of fibroblast growth factor -fibroblast growth factor receptor complex with molecular principles of protien-protien interactions derived from the structural similarties between interleukin-1 and fibroblast growth factors will be presented.

PL2

Molecular recognition in relation to certain oligonucleotide and protein structures

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The possible reasons for thermal stability of the xylanases isolated from the thermophilic fungi *Thermoascus aurantiacus* and *Paecilomyces varioti* Bainier are analyzed in terms of additional disulfide and salt bridges and presence of the weaker C-H...O hydrogen bonds and C-H...π type interactions. The decamer d (GGGGCGCCCC) has two A-DNA duplexes in the asymmetric unit and the structural differences appear to originate from an inherent propensity of the sequence for varied intermolecular interactions and malleability. A 3.1Å single crystal x-ray data point to an intercalated tetraplex structure for d(CCCCAACCCCAA) with hemi-protonated C.C$^+$ base pairs for the C-stretches.

References:
R.Natesh, P.Bhanumoorthy, P.J.Vithayathil, K.Sekar, S.Ramakumar and M.A.Viswamitra, JMB (1999) 288, 989.
P.Rajesh Kumar, S.Eswaramoorthy, P.J.Vithayathil and M.A.Viswamitra (unpublished).
G.Savitha, D. Leonidas, K.R.Acharya and M.A.Viswamitra (unpublished).
G.Savitha and M.A.Viswamitra, Acta Crystallographica D (1999) (under print).

PL3

In vivo NMR of Neurotransmitter Fluxes

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Biophysics has always played a major role in neuroscience. Recently nuclear magnetic resonance studies of brain imaging and the underlying neurochemistry have continued this tradition. NMR imaging methods have localized brain activity extending measurements by other imaging modalities. These imaging methods depend upon neurophysiological changes e.g. metabolism of glucose and oxygen as well as upon the associated changes in blood flow (1). Recently changes in rates of glucose oxidation have been shown by in vivo ^{13}C NMR to be stoichiometrically coupled to a particular cortical neurotransmitter flux(2). Simultaneous ^{13}C NMR measurements of the rates of glucose oxidation and glutamate/glutamine neurotransmitter cycling have revealed a 1:1 stoichiometry between these two fluxes. Accordingly it has been possible to derive quantitative measurements of a specific neurotransmitter activity from the rates of glucose oxidation revealed by functional imaging signals. These results show that the mammalian brains, human and rat, in the absence of external stimulation, show very active neurotransmitter activity and that during stimulation this activity increases slightly in localized regions. This understanding provides boundary conditions for psychological concepts of mind, in ways that will be discussed (3).

1. Shulman, R.G. and Rothman, D.L., Proc. Natl. Acad. Sci. USA, 95:11993-11998 (1998).
2. Sibson, N.R. et al., Proc. Natl. Acad. Sci. USA, 95:316-321 (1998).
3 Shulman, R.G., Rothman, D L. and Hyder, F., Proc. Natl. Acad. Sci. USA, 96:3245-3250 (1999).

PL4

PROTEIN DYNAMICS EXPLORED BY NMR

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It is stressed in this lecture that one of the major strengths of NMR, as applied to biomolecules, is the possibility to explore molecular dynamics in great detail. Techniques are available to cover time ranges from seconds to picoseconds. Examples will be presented for a cyclic decapeptide, antamanide, and for a small protein, human ubiquitin. The dynamic processes to be covered concern backbone and side-chain motions as well as folding and unfolding processes under various temperature and pressure conditions.

PL5

Calcium Signals and Short Term Synaptic Plasticity

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Plastic changes in the connectivity between neurons underly the adaptive information processing of the central nervous system. The shortest forms of such plasticity are synaptic depression & facilitation, which happen on the subsecond time scale. If synapses are stimulated repetitively at intervals of 10 to 100 ms, some types depress (second and third response is smaller than the first one), others facilitate (responses are increasingly larger). This behaviour has been studied extensively in the 1960's and 1970's and depression in most cases has been attributed to depletion of a pool of 'release ready vesicles', while facilitation has been connected to 'residual Ca^{++}' i.e. the Ca^{++} remaining in the terminal following a first stimulus, onto which the Ca^{++} inflow during subsequent stimuli superimposes. Obviously, the two mechanisms might mutually occlude each other. Unfortunately, a quantitative description was difficult, due to the smallness and inaccessibility of the nerve terminal. New techniques and new insights into the nature of the Ca-signal now allow a new look at these questions (see Neuron 20, 389-399, 1998, for review). Data from the Calyx of Held will be presented. This is a mammalian CNS synapse, in which both the pre- and the postsynaptic side can be voltage-clamped. The results will be discussed in terms of vesicle depletion (as the main cause for depression) and the influence of Ca^{++} buffers on facilitation will be considered.