P2.2.136   ESTIMATION OF THE AVERAGE ENERGY INCREMENT BY AMINO ACID EXCHANGE IN PROTEINS AND ITS USE IN EVALUATING A HOMOLOGY SCORING MATRIX. <u>S. Miyazawa</u>,, R. L. Jernigan*, National Institute of Genetics, Mishima, Shizuoka 411, Japan; *National Cancer Institute, National Institutes of Health, Bethesda, MD 20892, USA.

     In a previous study[1], we estimated the effective interresidue contact energy of each type of amino acid pair for proteins in solution from 18192 residue-residue contacts observed in 42 globular proteins. By using these contact energy and the number of contacts for each type of amino acid pair, we evaluate the average energy increment of protein native structures by an amino acid exchange. The estimates of average energy increments of exchanging each of the 20 kinds of amino acids for any other show reasonable characteristics of physico-chemical similarities of amino acids, and may be used to assess structural similarity of protein sequences. However, to consider the evolutionary relationship of protein sequences, base mutation rates and the effects of the genetic code must be taken into account as well as the conservative selection for amino acid exchanges. A transition probability matrix of codon substitutions and then a scoring matrix are evaluated to measure sequence homology. Codons are assumed to mutate to another codon with the probability proportional to the equilibrium frequency of the codon, only if it can occur with a single base mutation. The average fitness of an amino acid exchange is approximated by the average degree of instability of the protein structure, which is approximately equal to the Boltzman factor of the average energy increment by the amino acid exchange. The estimated scoring matrix is comparable to the Dayhoff's one. Results are discussed. Reference: (1) Macromolecules *18*, 534-552, (1985).

P2.2.137   THE INSULIN A AND B CHAINS CONTAIN SUFFICIENT STRUCTURAL INFORMATION TO FORM THE NATIVE MOLECULE. Chih-chen Wang* and Chen-Lu Tsou**, *DBB, CBER, FDA, Bethesda, MD 20892, USA; **National Lab. of Biomacromolecules, Acad. Sin., Beijing, 100080 China.

     Although 30-50% yields of insulin have been obtained by oxidation of its reduced chains in our and other laboratories, some authors still claim that, in contrast to the good yield in the case of proinsulin, very little insulin can be obtained or about that to be expected from random joining of its chains considering only the A_1B_1 isomers implicating that C peptide provides the structural information. However, the formation of oligomeric products containing any number of one or both chains should be considered leading to the total number of all possible products being infinity. By treatment of either the separated chains or the scrambled molecule with protein disulfide isomerase, we have now obtained about 30% of insulin recovery which is also much higher than expected by random joining of the chains. Moreover, the addition of C peptide has no appreciable effect. Insulin chemically cross-linked through A_1 to B_{29} containing native disulfide linkages can be obtained from the scrambled, the S-sulfonated or the reduced molecule with yields up to more than 90%. As it is most unlikely that different chemical crosslinking reagents can all provide the same structural information, it appears that insulin A and B chains do contain sufficient information and the role of the C peptide, like the crosslinking reagents, is to bring and to keep the two chains together. HPLC analysis shows that the products formed from the chains contain three major peaks which are inactive products composed of A or B chain alone, respectively, and insulin with full activity. There are other minor peaks, but of those containing both chains insulin is the only predominant product and hence the most stable.

P2.2.138   SIMULATION OF HELIX ASSOCIATION IN MEMBRANES. <u>H.R. Treutlein</u>, D.M. Engelman, A.T. Brünger, Department of Molecular Biophysics and Biochemistry, Yale University, 260 Whitney Avenue, New Haven, CT, USA 06511

     We have developed a method for investigating energetic properties of helical protein structures associated inside a membrane. The method assumes a coiled-coil conformation of the helices. The helices are rotated against each other and their interaction energy is calculated as a function of the rotation angles around each of the two helix axes. The XPLOR program is used for rotating, equilibrating the structures and for energy calculations. Special restrains for backbone atoms are introduced to keep the helices in a coiled-coil conformation during all calculations. The method was tested in the case of the known structure of the helix association in the CAP dimer, a globular protein [Banner, D.W. et al, J. Mol. Biol., 196(1987) 657]. The results of our calculations for the unknown structure of the transmembrane portion of the Glycophorin A dimer [Welsh, E., Thom, D., Biopolymers, 24(1985) 2301] suggest the possibility for the prediction of helix orientation in membranes.

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