PL-1

Computational Biology to Understand Genome and Transcriptome

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PL-2

Structural insights into SARS coronavirus replication machinery

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Zihe Rao's group has been active in SARS basic research since the 2003 global outbreak, and was the first to determine the crystal structure of a key replicase protein encoded by the SARS coronavirus (SARS-CoV) - the main protease or Mpro - and its complex with an inhibitor. His group has since made a number of important breakthroughs in SARS research, and the major achievements include: wide spectrum inhibitor design targeting coronavirus Mpro; the elucidation of the autocleavage mechanism of coronavirus Mpro; the structures of the spike (S) protein fusion cores from SARS-CoV and MHV; the structure of the super-complex between two SARS non-structural proteins, nsp7 and nsp8; the dodecamer structure of the SARS non-structural protein nsp10; and the hexamer structure of the MHV non-structural protein nsp15, an endoribonuclease. With more than 18 protein and complex structures from SARS-CoV and related coronaviruses to date, Zihe Rao's group has provided important structural insights into coronavirus replication/transcription.

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PL-3

Conformational Preferences of Proline Residue and Its Derivatives

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We report here the results on Ac-X-NHMe (X = Pro, Hyp, Oxa, Aze, and Pip) and oligoprolines (Ac-(Pro)$_n$-NMe$_2$, n = 1 to 5) as models for the proline residue and its derivatives as well as polyproline calculated using quantum chemical methods at the Hartree Fock (HF) and/or density functional (B3LYP) levels of theory to investigate conformational preferences and thermodynamic properties of the prolyl residue and its derivatives depending on the cis-trans isomerization and puckering in the gas phase and in solutions. In particular, by analyzing the potential energy surface and local minima, it is found that the prolyl ring flips from a down-puckered conformation to an up-puckered one through the transition state with an envelope form having the N atom at the top of envelope and not a planar one for both trans and cis conformers. The 4(R)-substitution by electron-withdrawing groups, the substitution of $^{\gamma}CH_2$ by O and S atoms, and the change of the ring size for prolyl ring result in lowering rotational barriers to the cis-trans isomerization. The barriers to the cis-to-trans isomerization for all dipeptides increase as the increase of solvent polarity. In particular, it is identified that the cis-trans isomerization proceeds through the clockwise rotation about the prolyl peptide bond in chloroform and water. It is confirmed that the transition of polyproline II with all trans peptide bonds to polyproline I with all cis peptide bonds is initiated at the C-terminal and proceeds to the N-terminal in water.

PL-4

Biophysical basis of cell electroporation with implications to improvement of cancer radiotherapy

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Biophysical understanding the effects of electromagnetic fields on biological systems has been considered important both from basic and practical viewpoint. In recent years studies on exposure of biological cells to high intensity but brief electrical pulses (a few kV/cm) beyond a threshold value has been shown to induce dramatic transient increase in the permeability of plasma membrane which allows entry of otherwise impermeant exogenous molecules into the cell. This phenomenon, called electroporation, has opened many new possibilities of cellular manipulation which has shown promise to develop a variety of new applications in biology and medicine. Electroporation allows gaining direct entry into the cell interior without seriously compromising cellular viability. In our laboratory extensive studies have been carried out on electroporation of red cells, CHO cells in culture and plant cells *in vitro* which have revealed invaluable data on nature, life time and resealing properties of induced micropores required for optimization of incorporation of drugs/other agents. Research results have shown great prospects for electroporative drug and gene delivery to target cell which may lead to novel biomedical applications such as, gene therapy, drug delivery. More recent studies on tumor cells in our laboratory have shown enhanced cytotoxic effects of ionizing radiation and anticancer drugs in combination with electroporation pointing to a new approach to improve cancer chemotherapy. This talk will present an overview of biophysical basis of electroporation and emerging new strategies for improvement of cancer radiotherapy.