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CENTRE FOR RESEARCH IN MOLECULAR MODELING
and the
DEPARTMENT OF CHEMISTRY AND BIOCHEMISTRY

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Mechanisms for Oxidative Damage to Proteins:
Computational Modelling
and Relevance to Alzheimer's Disease

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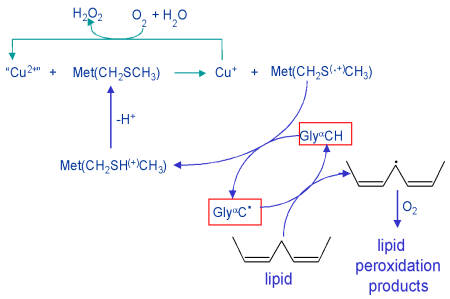
Damage to proteins due to H-atom abstraction by reactive oxygen radicals and thiyl radicals has been examined by ab initio calculations of the reactant, product, and transition structures involved. The surprising prediction that thiyl radicals may cause damage at the alpha-C site of every amino acid residue has been confirmed by experimental studies on model peptide residues. Alpha-helical secondary structure confers complete protection to the backbone. In beta-sheet secondary structure, all residues are protected from backbone damage except glycyl residues. Generation of free radicals by redox chemistry of bound copper ions has also been examined. A mechanism is proposed whereby one electron oxidation of the single methionine residue of the beta amyloid peptide begins a cascade of free radical damage that results in the degradation of cell walls and cell death. Such a mechanism may be the ultimate chemical cause of neurological diseases like Alzheimer's Disease, prion diseases, and possibly others.



Arvi Rauk graduated in 1965 from Queen's University, where he also obtained a Ph.D. in 1968. He then went to Princeton University for two years as a Research Associate before taking up an Assistant Professor position at the University of Calgary. Dr. Rauk became Professor in 1980 and Faculty Professor in 2000. He has collected numerous fellowships; he was named a Killam Resident Fellow in 1980 and Fellow of the Chemical Institute of Canada in 1991. Dr. Rauk has published over 170 research articles and chapters, and is an Editor of the Canadian Journal of Chemistry.