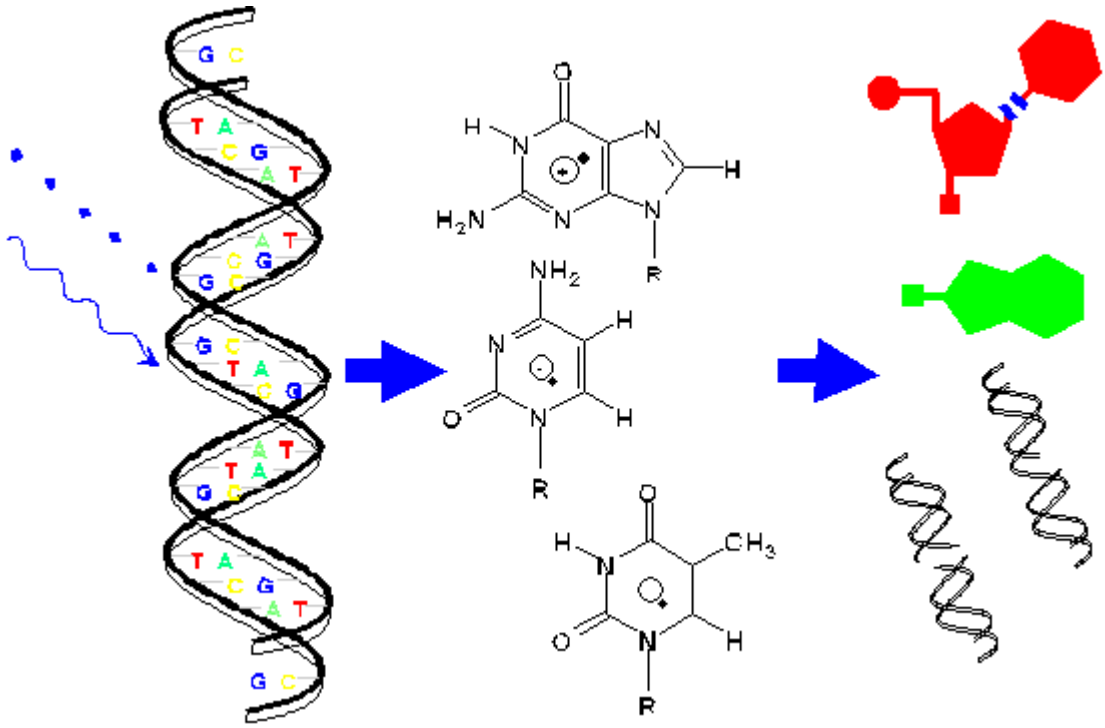
Molecular mechanisms of the effects of ionizing radiation: free radicals from DNA and model compounds

For the investigations of the interactions of ionizing radiation with organisms or cells the DNA as carrier of the genetic informations is the centre of interest. The lesions of the critical target DNA are of great importance for the survival. The damage of DNA arise both from direct radiation action as well as from the indirect effect via water-radiolysis products. Direct radiation action involves deposition of the energy in the target molecule itself. The energy deposition in both the target molecule and the matrix leads to excitation or ionization. These pathways generate short-lived, primary and secundary radicals which are studied by Electron Paramagnetic Resonance (EPR) spectroscopy.
Since cells may contain a great number of radiation induced radicals, DNA and its constitutents (bases, nucleosides and nucleotides) are used as models. For modelling the direct or indirect effect various matrices for the sample are employed. Chemical modifications (e. g. specific deuteration) help to correlate EPR patterns with radical structures. The diamagnetic successors of the radicals, e. g. free bases after irradiation of nucleotides are separated with HPLC and detected by Nuclear Magnetic Resonance (NMR) spectroscopy.
One of our specific research interests is the investigation of the mechanisms of heavy ion bombardment which is used for therapy, especially of brain cancer. Models for the energy deposition and its action in the pathway of the heavy ion in the material are investigated. The radical structures, influences on the secundary products and the structure and yields of the diamagnetic products are determined.
Besides EPR spectroscopy the techniques of high resolution (pulsed EPR, high field EPR, ENDOR, pulsed ENDOR) are employed.



Structure-function relationship in metalloproteins: coordination of transition metal ions in proteins and model complexes

Electron Paramagnetic Resonance (EPR) spectroscopy and its high resolution techniques Electron Nuclear Double Resonance (ENDOR) and pulsed EPR spectroscopy are important methods for the investigation of the coordination sphere of transition metal ions in metalloproteins. Such proteins play a central role for the activation of small inorganic molecules (O_2, N_2, etc.) and are of great importance for a number of fundamental biochemical processes (photosynthesis, nitrogen fixation, oxygen detoxification). Spin density calculations and simulations with distance and angle variations using the experimental hyperfine interactions allow to investigate the coordination sphere (ca. 6 Å) with a resolution of about 0,1 Å in polycrystalline samples at low temperatures (about 4 K). This gives new insight in the structure-function relationship of metalloproteins.
With these methods, a number of proteins, especially copper proteins (superoxide-dismutase, azurine, alcohol-dehydrogenase), iron-sulphur proteins (enoate-reductase, APS-reductase, HiPIP-proteins), heme proteins (cytochrome P 450, hemo- and myoglobin) und proteins with molybdopterine cofactors (quinoline oxidoreductase, isoquinoline oxidoreductase) are presently investigated. The focus of interest is the structural change of the coordination sphere when ligands and/or inhibitors are bound.