Cytochrome c plays a central role in the mitochondrial respiratory chain. Highly productive and reproducible procedures have been developed to obtain the crystals of various cytochromes c and their mutants at low ionic strength. It allows us to address various aspects of cytochrome c function as well as those raised by a range of studies of the protein as a model system. One fundamental question is the basis for the structural stability of proteins. The crystal structures of the cytochromes c from horse and rat, along with several site directed mutants of the latter, were solved and refined at high resolution. Detailed comparison of the horse, rat and yeast cytochrome c structures revealed some structurally minor yet functionally fundamental differences between them. This suggests the necessity of studying the protein from taxonomically different origins to better understand the relationship of stability with function.

Based on modelling studies we proposed a mechanism of structural stabilization by His-26 both globally and on the local level. The major role was attributed to two hydrogen bonds bridging the middle and the bottom loops on the right side of molecule. The structures of the H26N, H26V, H26V/H33F and H26N/H33F mutant proteins examine the extent of success of these predictions.

To better understand the mechanisms for stabilizing the protein and for setting its unusually high reduction potential, the structures of several other single and double mutants on both sides of the heme prosthetic group are currently being refined. These studies will enable us to investigate synergism and antagonism between the effects of these mutations.

Human cytomegalovirus (hCMV) protease is synthesized as a 709 amino-acid precursor which undergoes at least two autolytic cleavages. The mature protease is one of the autolytic products and is composed of the first 256 amino acids of the precursor. The active center of the hCMV protease has been proposed to contain a serine, a histidine, and a glutamate although there is no sequence homology between this protease and known serine proteases. Recent studies have showed that only the homodimeric form of the protease is active [1].

Single crystals have been obtained in our lab employing the vapor diffusion technique. These crystals grow up to 0.25x0.25x0.6 mm in tetragonal morphology. Under X-ray irradiation, the crystals diffract to well beyond 2.8 Å Bragg's resolution. The cell constants are a=b=75.61 Å, and c=214.61 Å in the space group of P41212 (or P43212). There are two monomers per asymmetrical unit. A native data set has been obtained at room temperature with an Rmerge of 9.02%.