The nitro group of NAPD was clearly bound to those complexes in a typical fashion, but the density for the nitro group was not visible. That portion of the cofactor was disordered but appeared to reveal that the active site of thrombin has one anionic subsite (S1) and two hydrophobic subsites (S2 and S3) in addition to the catalytic site (Ser-195 and an oxyanion hole).

We have determined the three-dimensional structure of human cathepsin K in complex with the cysteine protease inhibitor E-64 at 2.2 angstroms resolution. The complex crystallizes in space group P21, with unit cell dimensions a = 38.4, b = 50.7, c = 104.9 Å. The structure was solved using molecular replacement with the coordinates of papain as the basis for a search model. The resulting electron density confirms that cathepsin K has the identical secondary structure and the same overall fold as papain. The position and conformation of the E-64 inhibitor are clearly evident. We will describe the structure of cathepsin K including the active site of the enzyme and the interactions with the inhibitor and compare this structure with other known cysteine proteases. Knowledge of the structure of cathepsin K will be useful in the structure-based design of inhibitors of the enzyme.

**Muscle & Motor Proteins**

**MS04.13.01 STRUCTURAL BASIS OF MYOSIN MOTILITY.** I. Rayment, A.J. Fisher, C.A. Smith, A. Gulick, R. Smith, H.M. Holden and K. Sutoh. Institute for Enzyme Research and Department of Biochemistry, University of Wisconsin, Madison WI 53705, and Department of Pure and Applied Sciences, University of Tokyo, Komba, Tokyo 153 Japan

The mechanism by which chemical energy is transduced into directed movement in muscle and myosin-based motility is a fundamental question in biology. Recently considerable progress has been made towards establishing the molecular basis of the sliding filament model that was proposed over 40 years ago through the determination of the three-dimensional structures of actin (Kabsch et al., 1990, Nature, 347, 37-44) and myosin subfragment-1 (Rayment et al., 1993, Science, 261, 50-58). These have provided a structural framework for a molecular hypothesis for muscle contraction (Rayment et al., 1993, Science, 261, 58-65). Even so many questions remain concerning the structural transitions that underlie the conversion of chemical energy into directed movement. In an effort to understand how ATP hydrolysis is coupled to movement we have determined the structure of a genetically truncated myosin head in the presence of more than seven substrate analogs including MgADP, MgATP, MgATP₂S, MgAMPNP, MgADP·BeF₄, MgADP·AlF₄, MgADP·VO₄, and several non-ATP derivatives that support tension. These complexes suggest a structural mechanism for ATP hydrolysis and new model for the conformational changes that underlie myosin-based motility.