A talk on the motor side. The free energy for mutating V186 and F244 to Leucine in beta-myosin and its ATP binding

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Hypertrophic cardiomyopathy (HCM) is clinically defined by the presence of a hypertrophic, nondilated left ventricle (LV) in the absence of an increased external load, and pathologically by myocyte hypertrophy, disarray, and interstitial fibrosis.
The clinical outcomes of HCM are highly variable, and range from asymptomatic benign course to hearth failure or sudden cardiac death (SCD). HCM is inherited as an autosomal dominant trait; approximately 2/3 of the patients have a family history of HCM or SCD, while in the reminder of sporadic cases the causing mutations arise de novo. During the last decades, more than 100 different mutations in 10 genes encoding contractile sarcomeric proteins have been identified in patients with HCM, the locus of beta-MyHC on chromosome 14q1 being firstly identified as a responsible gene for HCM. The beta-MyHC gene is comprised of 40 exons, and codes for a 6kb mRNA and a 220 kD protein. It is the predominant myosin isoform in the ventricle of large rodents and humans, comprising more that 90% of the total myosin in the human ventricles. Mutations in the beta-MyHC are the most common causes of HCM and account for approximately 35-50% of all HCM cases. Thus far, over 60 different mutations have been described, the majority of which are missense mutations located within the globular head of the myosin molecule.
As a contribution to the knowledge of the effects exerted by these mutations on the interactions involved at the molecular level, in this work we have carried out calculations on the relative free energy of binding of beta-myosin and its V186L and F244L mutants to ATP resorting to free energy perturbation methods using molecular dynamics.