Abstract Submitted
for the SES09 Meeting of
The American Physical Society

Computational Modeling of Molecular Effects of Mutations Causing Snyder-Robinson Syndrome[1] ZHE ZHANG, Department of Physics, Clemson University, SHAOLEI TENG, Department of Genetics & Biochemistry, Clemson University, EMIL ALEXOV, Department of Physics, Clemson University — Snyder-Robinson syndrome is an X-linked mental retardation disorder disease. The disease is associated with defects in a particular biomolecule, the spermine synthase (SMS) protein. Specifically, three missense mutations, G56S, I150T and V132G in SMS were identified to cause the disease, but molecular mechanism of their effect is unknown. We apply single-point energy calculations, molecular dynamics simulations and pKa calculations to reveal the effects of these mutations on SMS's stability, flexibility and interactions. It is demonstrated that even saddle changes as very conservative mutations can significantly affect wild type properties of SMS protein. While the mutations do not involve ionizable groups, still slight changes in the protonation of neighboring amino acids are suggested by the computational protocol. The dynamics of SMS was also affected by the mutations resulting in larger structural fluctuations in the mutant protein compared to the wild type. At the same time, the effect on SMS's stability was found to depend on the location of the mutation site with respect to the surface of the protein. Our investigation suggests that the disease is caused by diverse molecular mechanisms depending on the site of mutation and amino acid type substitution.

[1]The work was supported by grant from NIH, NLM, award R03LM009748.

Zhe Zhang
Department of Physics, Clemson University

Date submitted: 05 Nov 2009 Electronic form version 1.4