Abstract Submitted
for the MAR06 Meeting of
The American Physical Society

Quantum Mechanical Study of C-Terminal Cleavage Reaction in Inteins[1] PHILIP SHEMELLA, SAROJ NAYAK, BRIAN PEREIRA, SHEKHAR GARDE, GEORGES BELFORT, Rensselaer Polytechnic Institute - Troy, NY, PATRICK VAN ROEY, VICKY DERBYSHIRE, MARLENE BELFORT, Wadsworth Center - Albany, NY — Although inteins undergo autocatalytic cleaving and splicing reactions via a relatively well accepted reaction scheme, the mechanism that induces these reactions is not well understood. The reactions can be prevented or speeded up through mutations of various critical amino acids proximal to the active site or through changes in the solution pH and/or temperature. We are interested in obtaining an atomic level understanding of the C-terminal cleavage reaction using quantum mechanical reaction simulation techniques. The reaction is based on the highly conserved catalytic module of histidine-asparagine-cysteine. Experimentally, intein C-terminal cleavage occurs more readily at low pH and high temperature. Working closely with experimentalists, we use a combination of gas phase and implicit solvent techniques with density functional theory to compare energy barriers for various proposed mechanisms. The mechanism with the lowest energy barrier is consistent with experimental results and is based on the protonation of the peptide amide by a hydronium ion and the subsequent cyclization of the asparagine amino acid, resulting in cleavage of the peptide bond.

[1]Supported by NSF CTS03-04055-NIRT

Philip Shemella

Date submitted: 22 Nov 2005 Electronic form version 1.4