

## Abstract

### **Ab initio Molecular Dynamics Study on Influence of Noncovalent Interactions on Mechanochemical Reactivity of Disulfides.**

Deciphering the mechanochemical response of disulfides is of broad contemporary interest for multiple reasons: Today, disulfide bridges are known to not only serve as chemically inert molecular staples that stabilize protein structures, but redox-active disulfide switches (a.k.a. catalytic or allosteric disulfides) have been identified to take over prominent functions in the chemical regulation of enzyme activity via breaking and making of covalent S-S bonds. Beyond biochemistry, leaving disulfide bonds is central to rubber waste management where environmentally friendly scission of (di/poly)sulfide crosslinks and thus devulcanization can be achieved using mechanochemical activation. In functional materials, self-healable advanced elastomers capable of withstanding extreme mechanical stress by using dynamic crosslinkers and sacrificial bonds receive increasing attention.

Computations and bioinformatic analyses provide evidence that nonbonded interactions that originates from sulfur play important role in the structure and function of proteins.

In the project, we plan to focus on our preliminary discovery that the properties of disulfides encode at no stretching force the impact of noncovalent interactions, like chalcogen bonding and carbonyl-carbonyl interactions! These noncovalent bonds are increasingly recognized to be important not only in protein structure and interactions, but also begin to serve as a rational design tool in synthetic chemistry. The novel aspect to use chalcogen bonding in liquid-state synthesis has been highlighted in recent minireview by Huber and coworkers.

Our hypothesis is that this kind of nonbonded interactions and as we had previously communicated steric hindrance may be responsible to unexpected negligible acceleration of force-induced disulfide reduction in macrocycle molecules studied by Kucharski et al. experimentally.

The key aspects of the project – mechanical force, noncovalent interactions, solvent and temperature - will be considered by the *ab initio* molecular dynamics (AIMD). Our computational formalism is based on the concept of Force-Transformed Free Energy Surfaces.

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