ACTIVATION ENERGIES DEFINE KINETIC (IN)STABILITIES OF THERAPEUTIC ANTIBODIES

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Antibody degradation pathways are many-fold and can result in loss of function, efficacy and even to adverse effects in patients. Among others, aggregation and fragmentation is still the major challenge. The identification of the primary degradation pathway can be very complex. Monoclonal antibodies (mAbs) are large, multi-domain macromolecules. Due to their complex nature and inherent properties, temperature induced unfolding leads to rather complex unfolding kinetics. In this study, we determined activation energies (Ea) of thermal intrinsic fluorescence (IF) unfolding profiles unique for each individual antibody. The analyzed activation energies give insights both into kinetic (in)stabilities of single domains and the overall structure of the antibody. To realize this, we used a novel developed experimental setup to perform temperature dependent fluorescence unfolding profiles of various mAbs. In conclusion, the activation energies can be used as descriptors for kinetic (in)stabilities of therapeutic antibodies. Moreover, we show that lower activation energies correlate to monomer loss in long-term storage stabilities and can thus likely be used for shelf-life prediction.