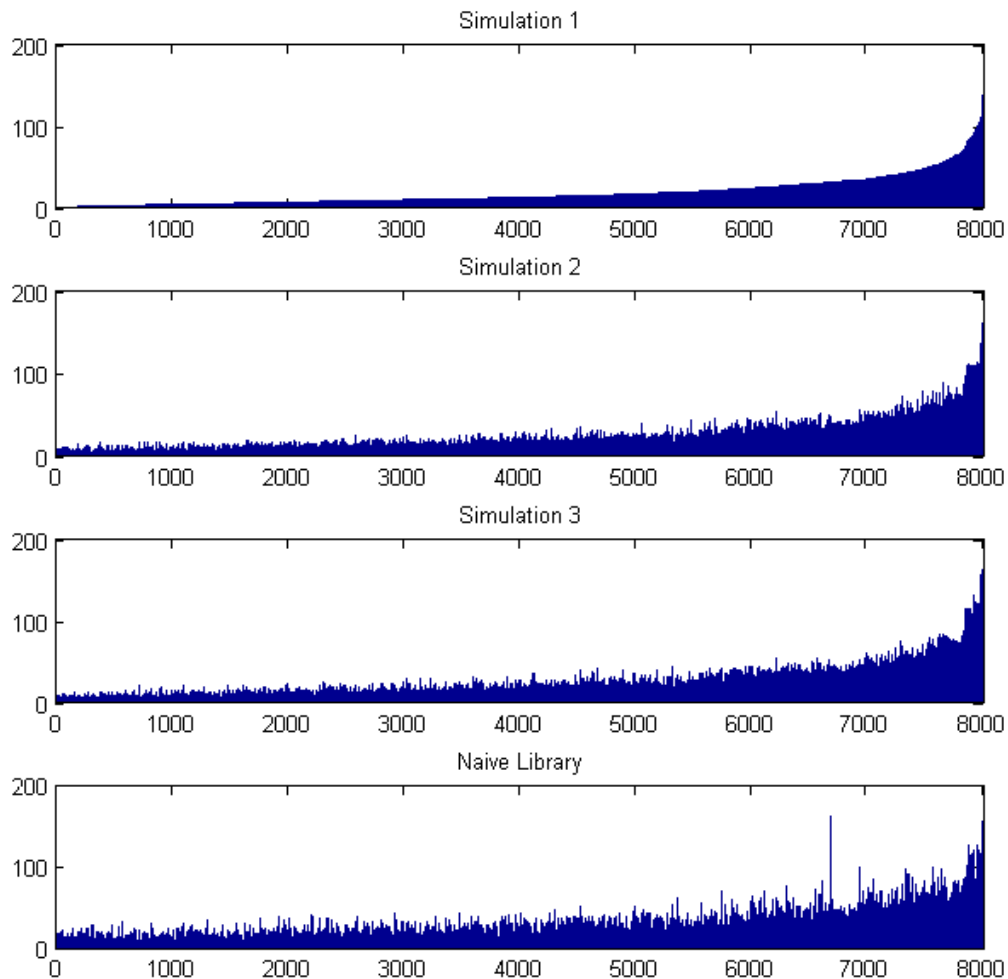


### Distribution of CaaX-Box Motives in the Naïve and Three Independently Simulated Libraries



**Figure S1:** In the naïve library, the count of 8000 theoretically possible individual CaaX-box motifs ranges from 0 to 153 within a total of 168,627 of NGS counts. This relatively large spread in the occurrence of individual CaaX-box motifs in the naïve library primarily arises from the different codon frequencies encoded by the degenerate NNS codons as three independently simulated CaaX-box libraries yield distributions that are comparable to the naïve library. Here, on average, the normalized fold-deviation of different CaaX-box motifs in Simulation 1 compared to Simulation 2 and 3 differs by 9% while Simulation 1 compared to the naïve library (for CaaX-box motifs occurring more than twice) differs by 28%.