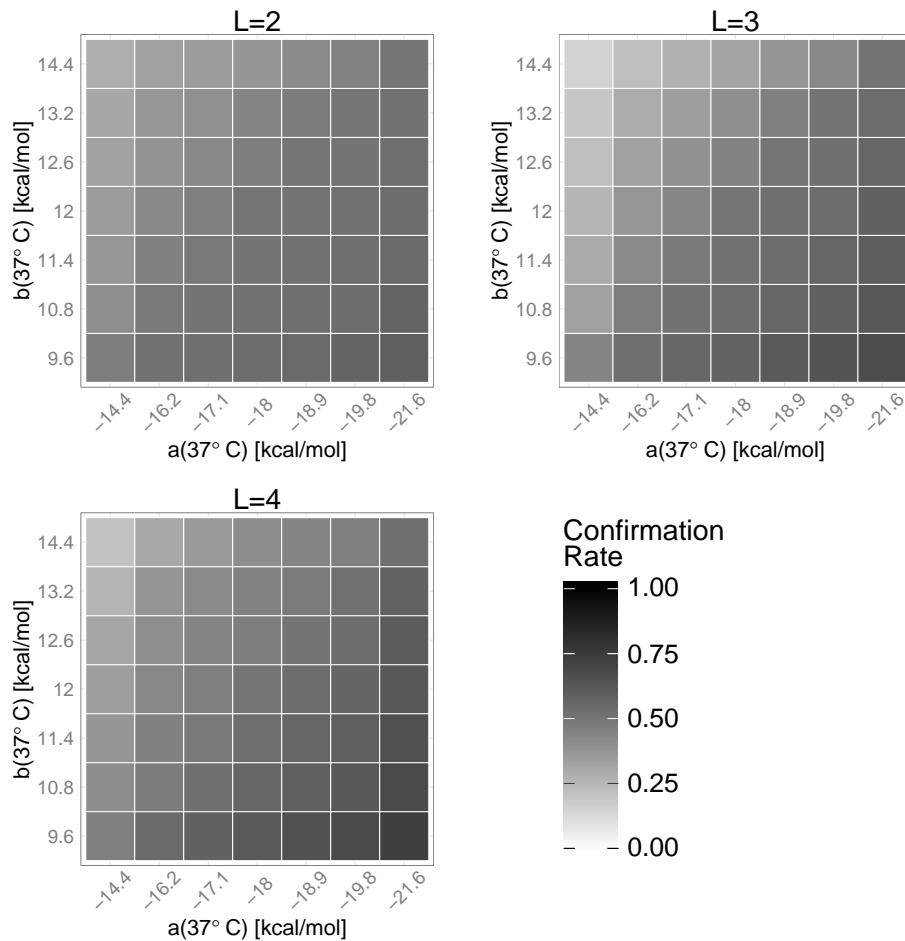


## Robustness of Energy Parameters

In order to test the impact of changes in the fitted energy parameters we consider two sets PQS with layersize 2, 3, and 4 from the human genome. For each layer size, we randomly picked 1000 loci that fold into quadruplexes with our standard parameters and 1000 loci that fold into alternative structures in our genome-wide RNAfold screen. Varying the parameters  $a$  (quadruplex stacking energy) and  $b$  (entropic contribution of the linkers) we record the number of loci at which quadruplexes are predicted. Not surprisingly, this number increases monotonously as  $a$  and  $b$  decreases. The effect seems to be largest for  $L = 3$ , where the parameters, which are based on measurements for  $L = 3$ , are most accurate.



Supplemental Figure 1.