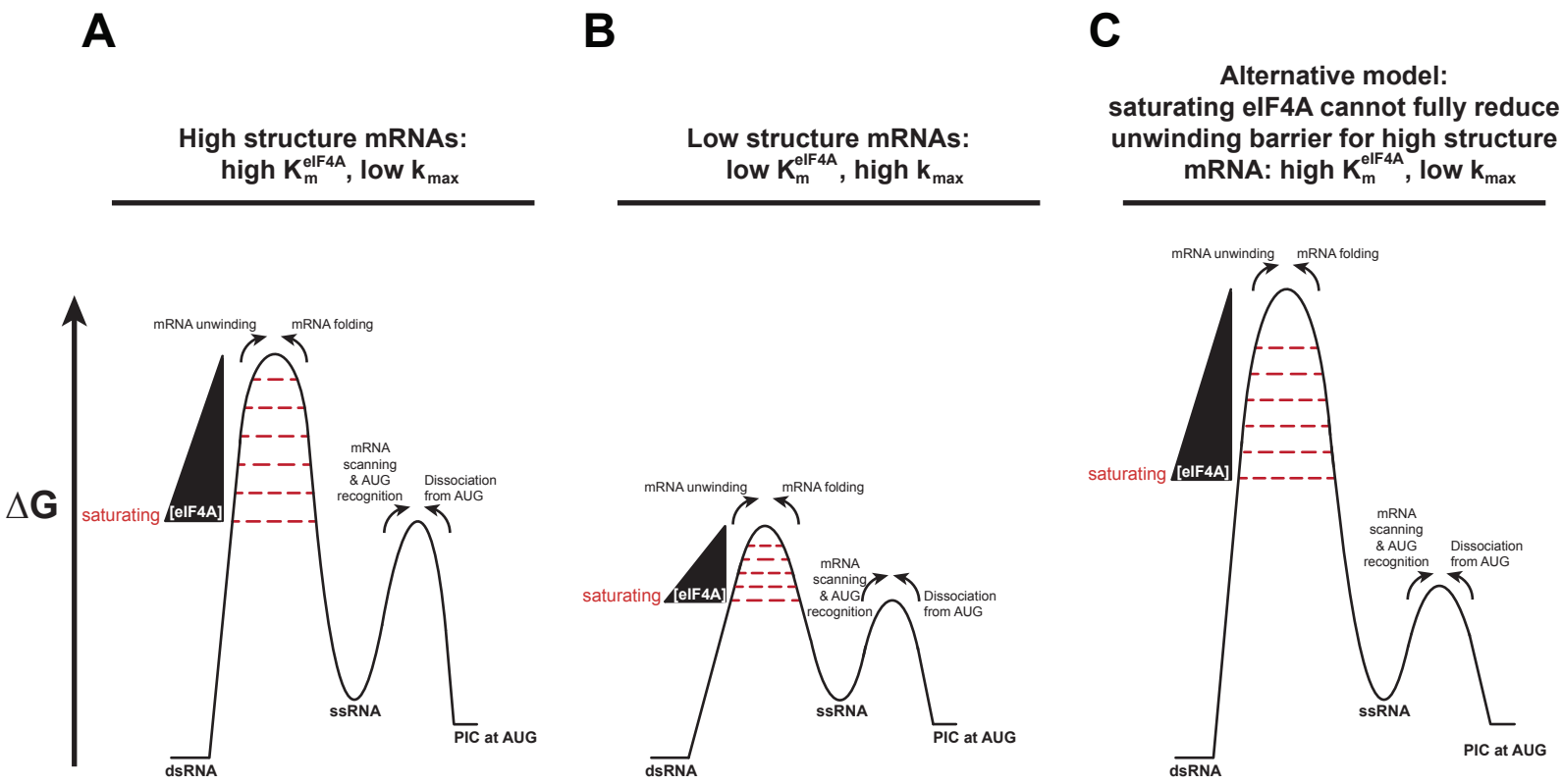

Figure 3 – figure supplement 3.

Figure 3 – Figure supplement 3. A change in the rate-limiting step for mRNA recruitment may be responsible for the effect of mRNA structure on the $K_{1/2}^{eIF4A}$ values. **(A)** An mRNA harboring a high degree of structure has a large barrier to mRNA recruitment posed by the need to resolve those structures in order to load the mRNA onto the PIC (left-hand barrier). As the concentration of eIF4A is increased, it decreases the height of this barrier by facilitating the disruption of the structures in the mRNA (wedge and decreasing barrier height). When the barrier posed by structure has been reduced below the level of the right-hand barrier for subsequent steps (e.g., scanning, AUG recognition) the latter, which is not dependent on eIF4A, becomes rate-limiting and the rate of mRNA recruitment plateaus as a function of eIF4A. This situation leads to a high value of $K_{1/2}^{eIF4A}$. (B) An mRNA with a low degree of structure has a small eIF4A-dependent barrier (left-hand barrier), which is reduced below the level of the barrier for subsequent steps (right-hand barrier) at a lower concentration of eIF4A than in (A). This situation leads to the plateau of the reaction rate occurring at a lower eIF4A concentration, which yields a lower $K_{1/2}^{eIF4A}$ value. To explain the different k_{max} values in these two situations, we posit that the barrier for the second, eIF4A-independent step is lower for mRNAs with little structure than for those with high degrees of structure. This scenario would make sense if this second step involves scanning of the mRNA, which would be inhibited by structures. (C) In an alternative model, which is also consistent with the data, eIF4A cannot lower the barrier for unwinding of mRNAs with high degrees of structure below the level of the eIF4A-indpendent barrier, even at very high eIF4A concentrations, leading to high $K_{1/2}^{eIF4A}$ values and low k_{max} values. In this case, the scenario for mRNAs with low degrees of structure could remain the same as in (B).