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An engineer's understanding of kinetochore motility and signaling

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The kinetochore is a macromolecular motor that couples chromosome movement to microtubule polymerization and depolymerization. It is also a mechanochemical signaling hub. A kinetochore that lacks microtubule attachment generates a biochemical signal to arrest the cell cycle. Both kinetochore functions require numerous copies of ~ 8 proteins and protein complexes. A cohesive explanation of how multiple kinetochore components cooperate to achieve motility and signaling remains elusive. I will describe on-going “architecture-function” analysis in my lab that applies an engineer’s perspective to study the machine that is the kinetochore. This analysis is based on the definition of the protein architecture of the kinetochore using known protein structures, copy numbers in the kinetochore, average positions, and distributions. This architecture enables us to assign specific functions to each kinetochore component in generating movement. The architecture also reveals the molecular mechanism of kinetochore signaling embedded within the kinetochore.