Review of: "Modeling the processive movement of dimerized kinesin-10 NOD motors"

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Potential competing interests: No potential competing interests to declare.

Ping Xie has developed theoretical models to explain the processive motion of dimerized kinesin-10 NOD motors and has shown the ATPase cycle of NOD motor in comparison to kinesin-1, in the article “Modeling the processive movement of dimerized kinesin-10 NOD motors”. The work is interesting and should be published. However, the manuscript needs to be rewritten with more clarity. Here are a few suggestions that author needs to provide with proper explanation.

1. *“This characteristic for the NOD head is in sharp contrast to that for the kinesin-1 head which shows the weak affinity in ADP state while in other nucleotide states such as* ***nucleotide-free and AMPPNP*** *states has the high affinity to MT”.* This paragraph in introduction should discuss the differences in affinity of kinesin-1 and NOD in their ATP-bound state. Specifically, the ATP bound state is not mentioned clearly.
2. Model-1 involves ATP bound motor domain as a weak binding state of motor domain with microtubule, and it causes the dissociation of motor from microtubule. There are no further associated conditions (ATPase activities) attached to the model-1. Rather, steps from model-1 are the initial steps for model-2. Model-2 discusses the different conditions of ATP bound domain as well as the domain with free-nucleotides. Hence, model-1 seems as an incomplete approach. Why do we call model-1 as a model?
3. (page 7) “*The NOD head in nucleotide-bound state has a much weaker affinity (Ew1) to the local tubulin having the* ***large conformational changes*** *than the weak affinity E(w2) to other tubulins without the large conformational changes*,” – the sentence needs to written better with clarity. Author describes that for kinesin-1, the large conformational changes is induced by the strong interaction of motor domain with tubulin. For NOD, what causes the large conformational change of local tubulin when the NOD is in the weak binding state?
4. “*A puzzling issue is that while after mixing of the ATP-head with MT the ATP-head can bind rapidly to MT, why after ATP binding to the nucleotide-free head the ATP-head can dissociate rapidly from MT*” – the sentence on page-9 is confusing and requires more clarity.
5. “This indicates that after ATP binding to the nucleotide-free NOD head, a very short time tr (in the order of μs) is present when the local tubulin has a very weak affinity Ew1 to the nucleotide-bound head and in tr, with the local tubulin restoring elastically to the normally unchanged form, its affinity to the nucleotide-bound head changes to Ew2, as argued for kinesin-1” – please revise the sentence.
6. ATP-bound state has weak affinity for microtubule for NOD motor. In model-3 (ATPase activity in the trailing head), the head with ATP continues from fig ‘a’ to fig ‘e’ (the blue head with ATP). This is misleading. Why the orange head with ATP has stronger affinity Ew2 with microtubule?

7. Section 4.1: the statement “high affinity **between two heads**” is probably misleading. Is it the high affinity of both heads interacting with microtubule?
8. Check for typos.