

# A role for the primary cilium in network properties of neurons

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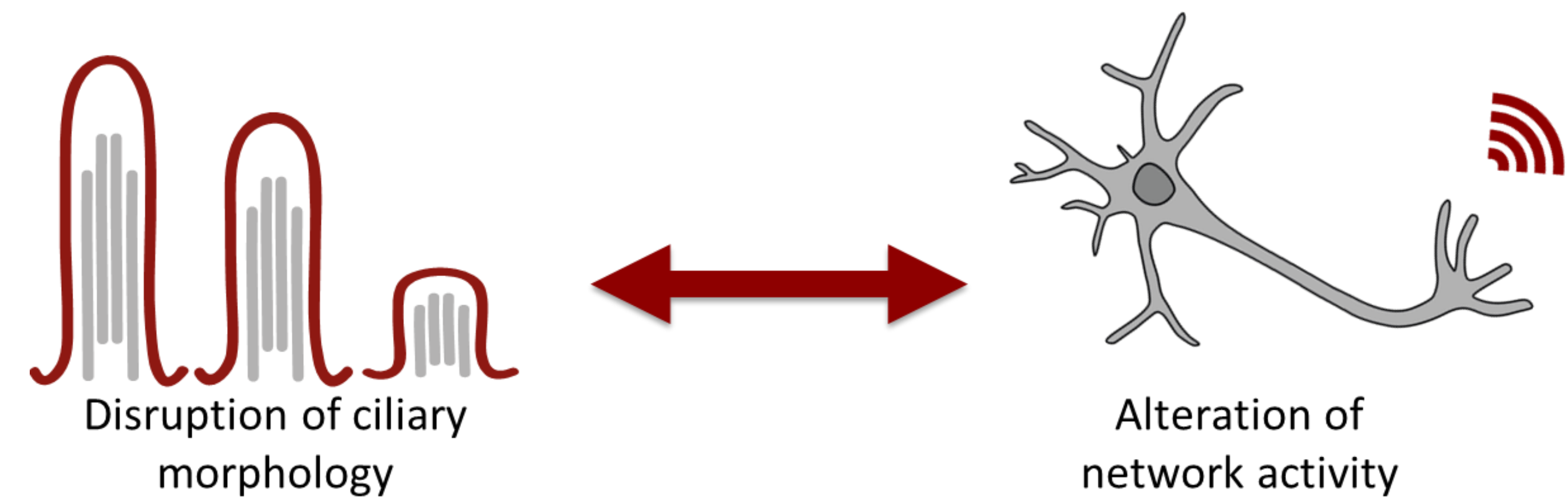
## Introduction

The **primary cilium** – often referred to as the cells' antenna - is a small organelle involved in a diverse array of signalling pathways. Dysfunction of the cilium results in a spectrum of developmental disorders including the neurodevelopmental disorder, **Joubert syndrome**. Up to 90% of neurons in the mammalian cerebral cortex are ciliated, yet the function of this organelle in excitatory neurotransmission has not been fully established.

We seek to:

- Further characterise the role of the primary cilium in establishing a neuronal network,
- Generate a model in which to study the role *Joubert syndrome*-related proteins play in network formation and maturation.

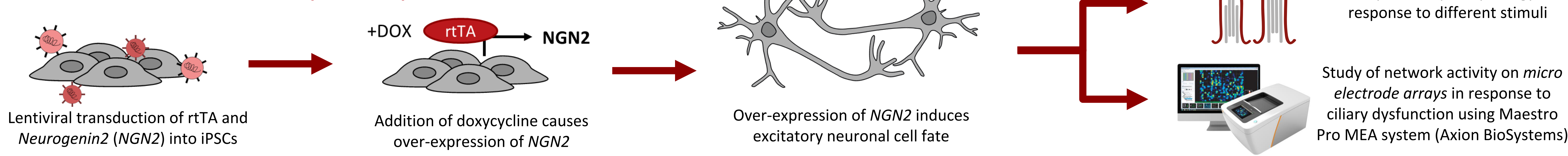
## Discussion and concluding remarks



The primary cilium is linked to the excitatory properties of *iNeurons* with morphological changes preceding and following abnormal network activity.

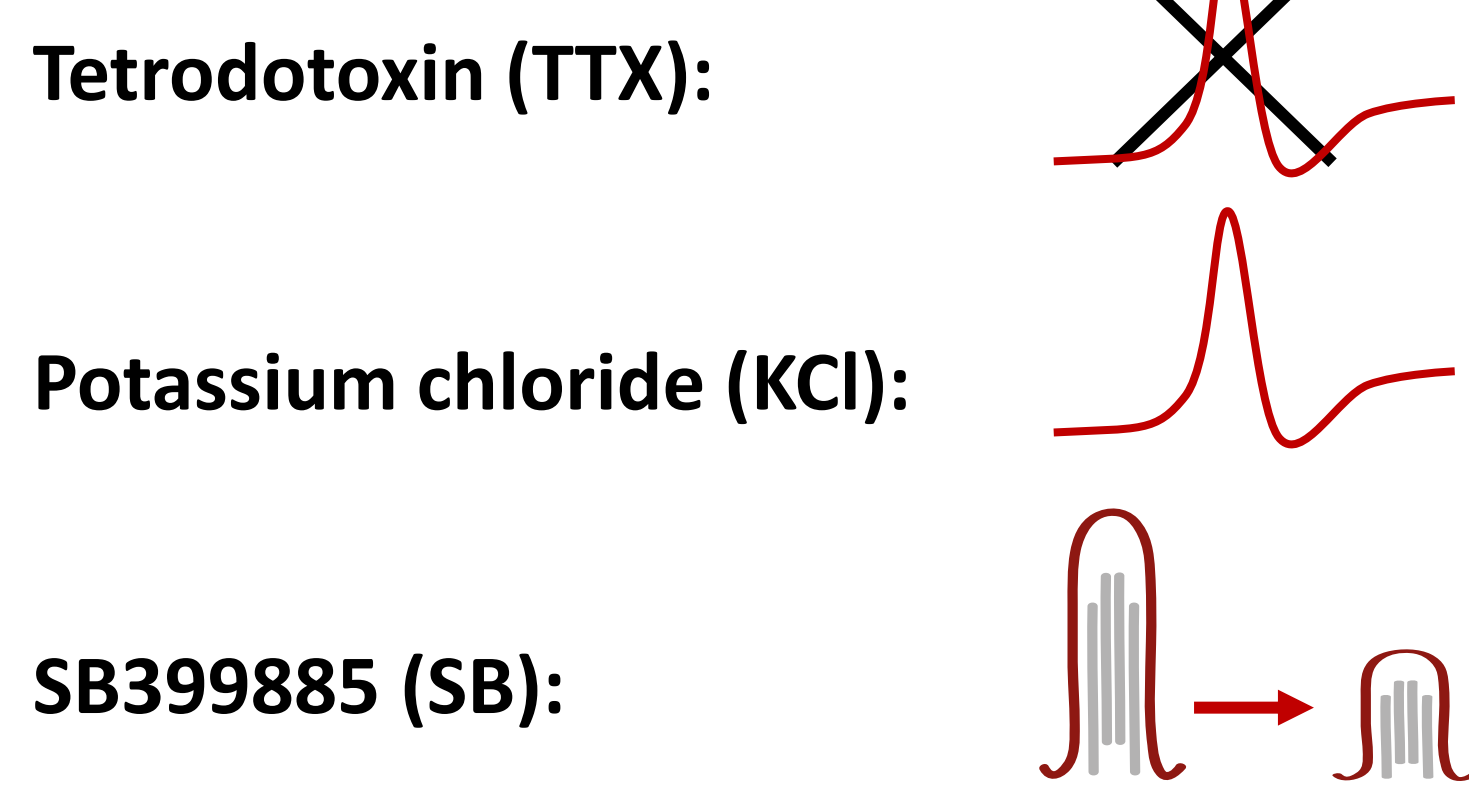
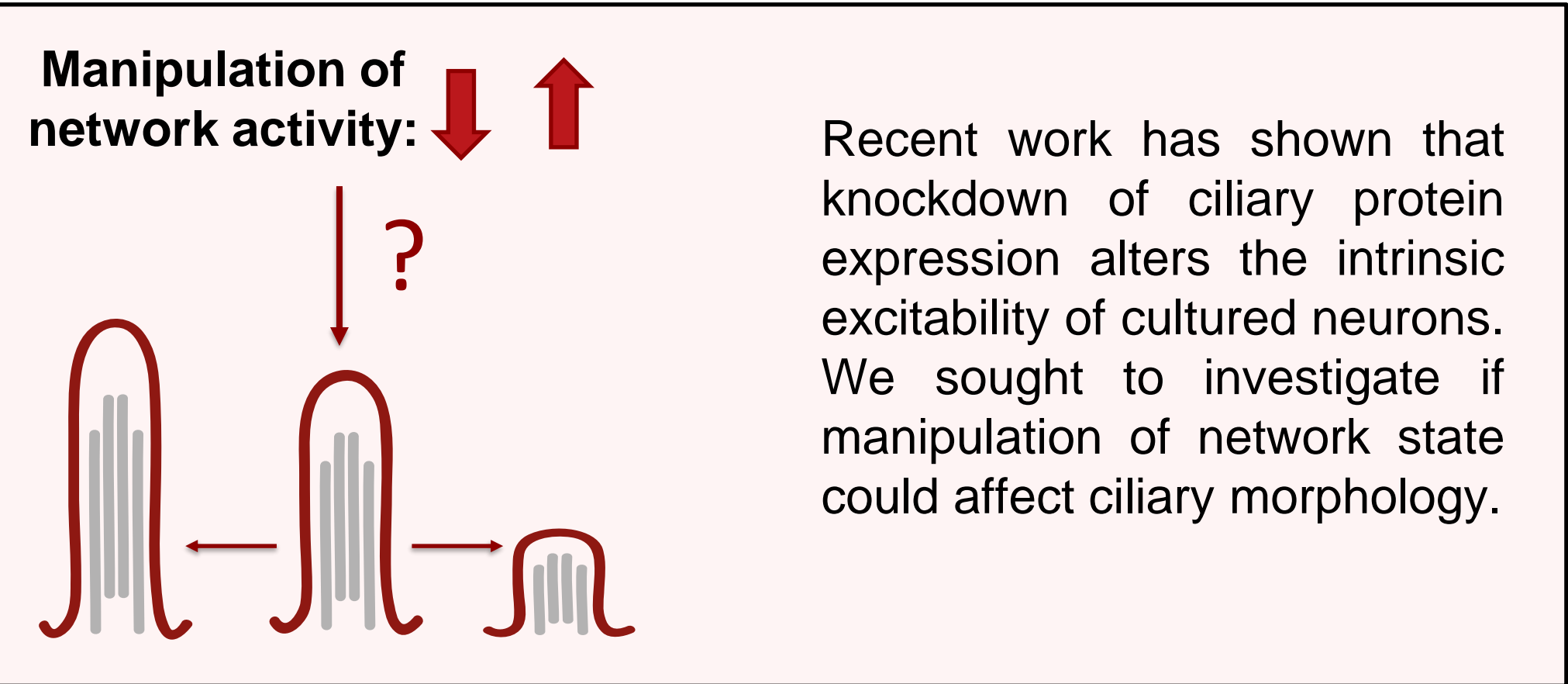
## Model system

### Generation of inducible neurons (*iNeurons*):

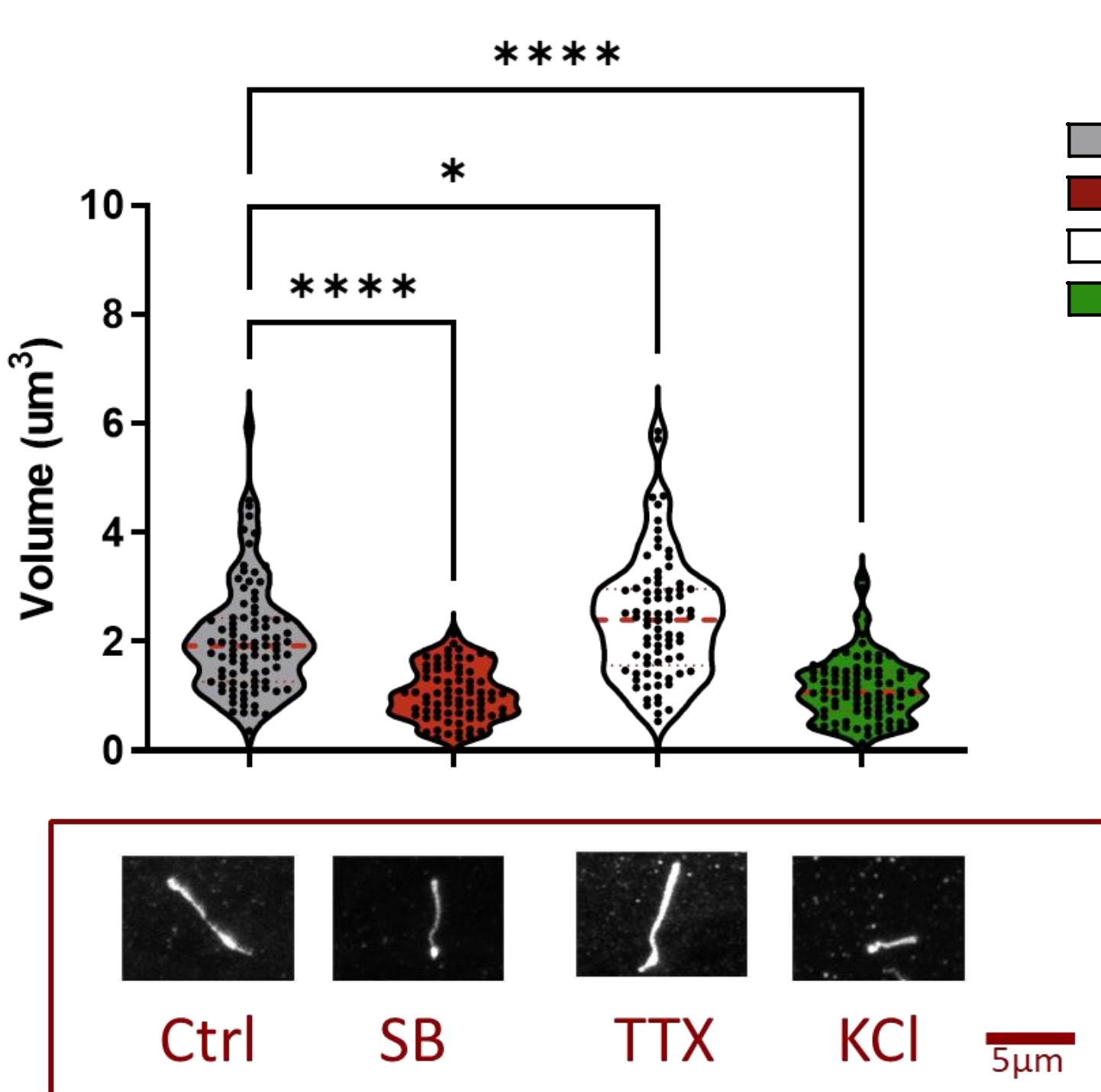


## Cilia respond to changes in network properties

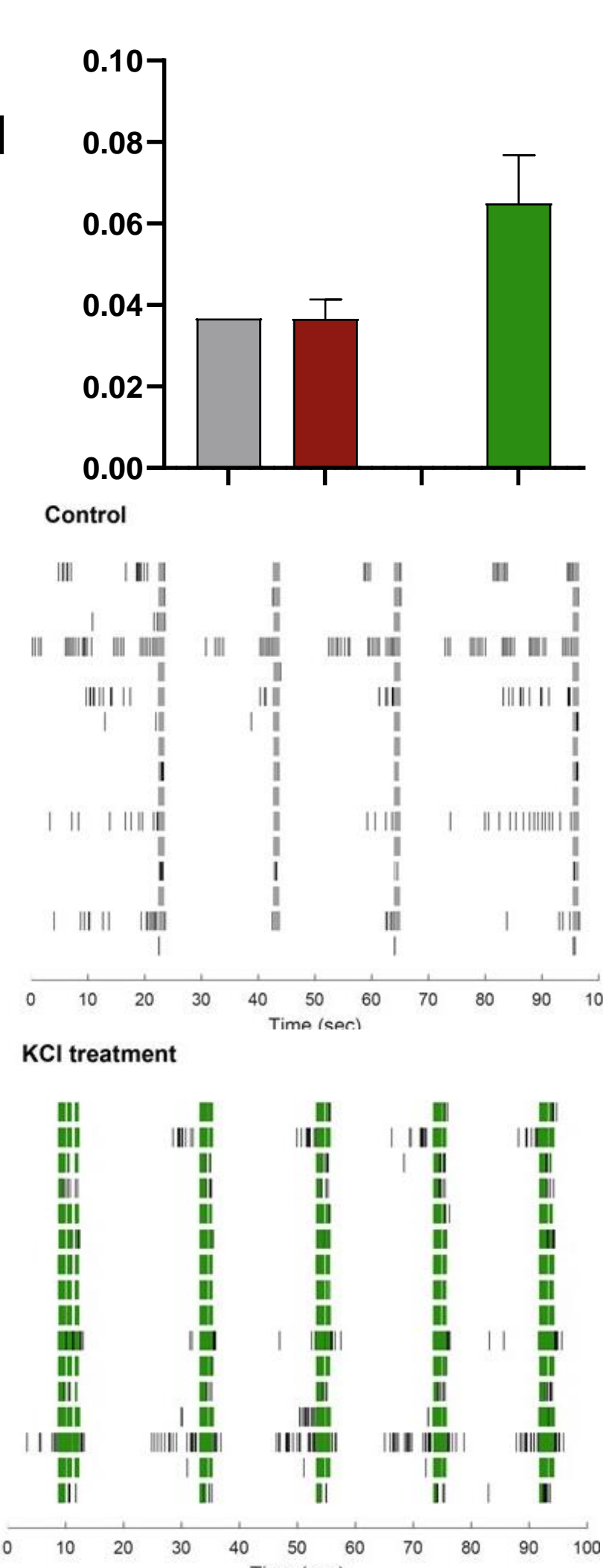
The primary cilia of *iNeurons* show bidirectional changes in volume in response to decrease or increase in activity:



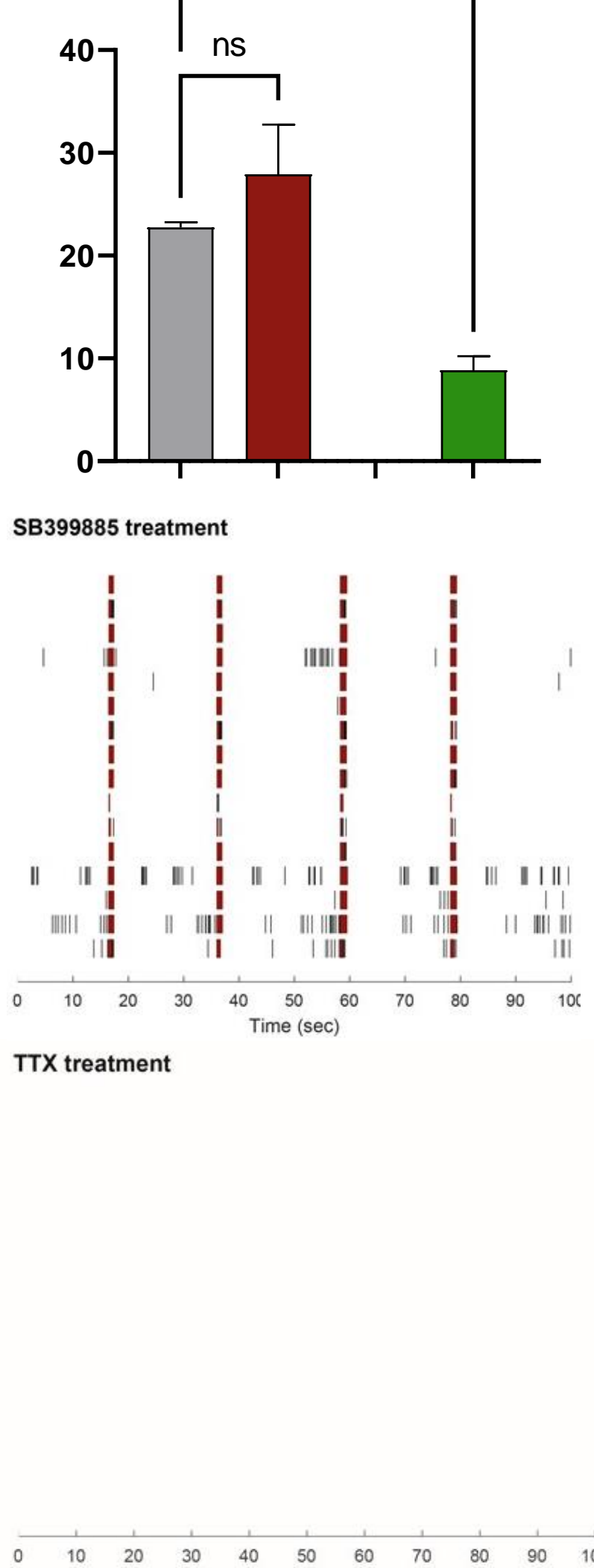
### Ciliary volume of treated *iNeurons*



### Network burst frequency

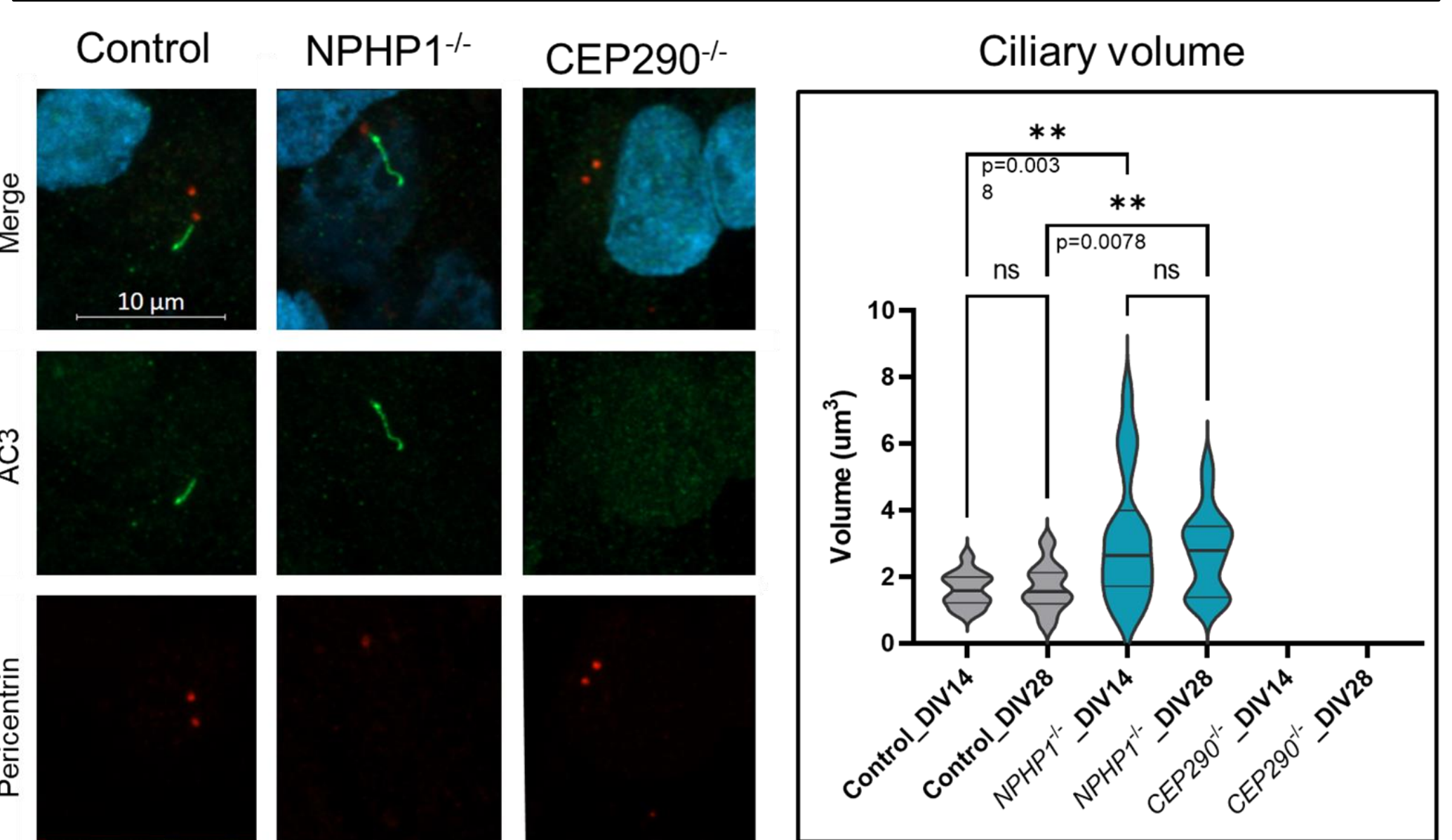
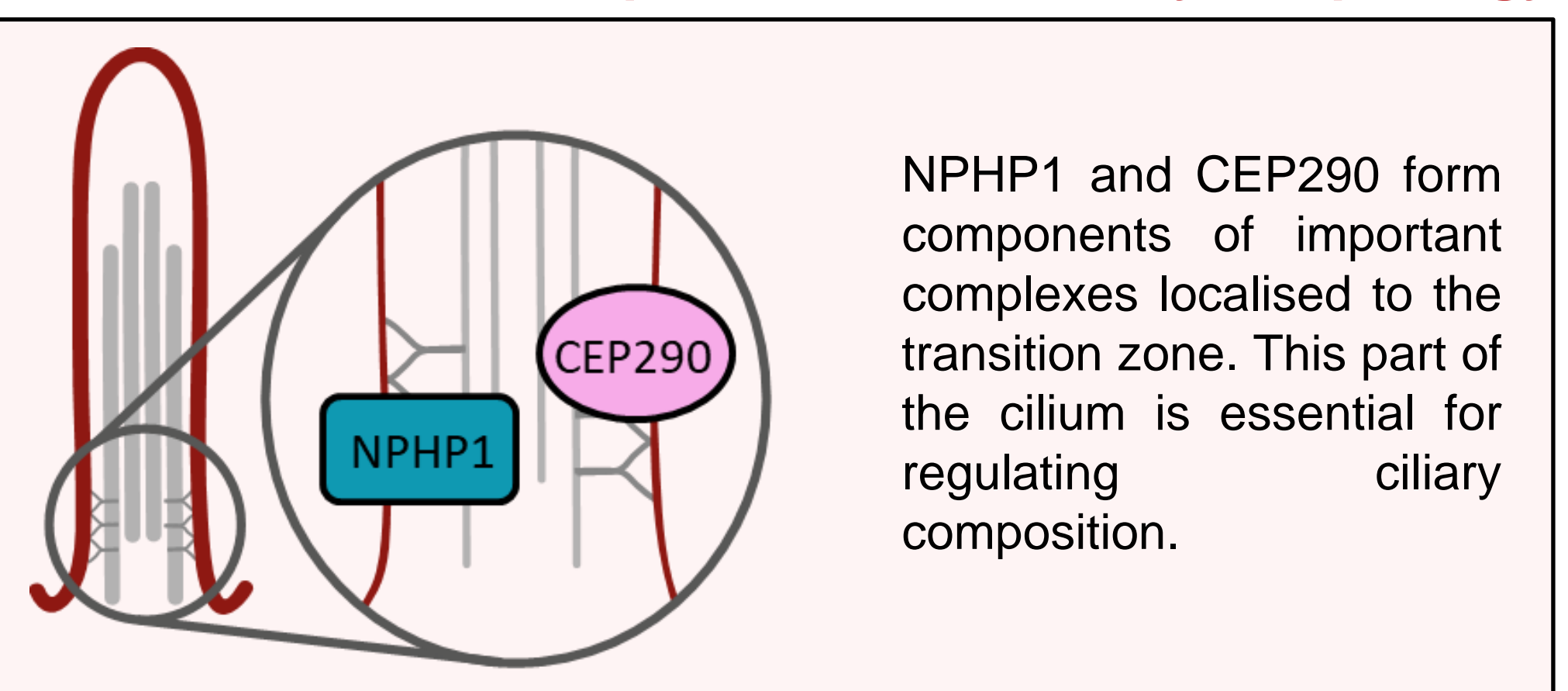


### Mean inter burst interval

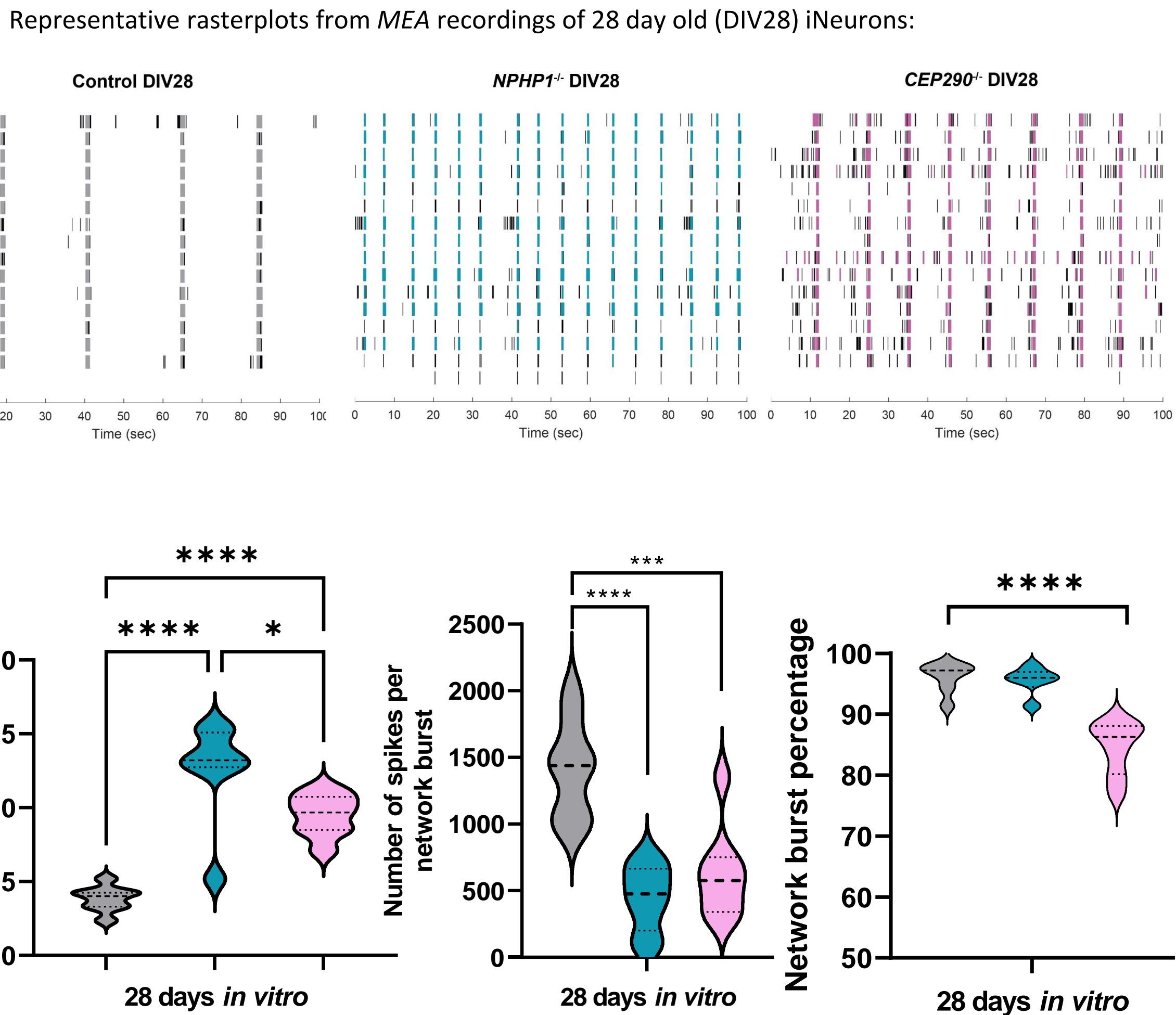


## Alteration of ciliation changes activity

### Loss of transition zone proteins alters ciliary morphology:



### *NPHP1*<sup>-/-</sup> and *CEP290*<sup>-/-</sup> derived *iNeurons* show increased network activity:



Loss of transition zone proteins CEP290 and NPHP1 leads to loss of cilia, and increase in ciliary volume respectively. Despite the opposite morphologies the cell lines display similar network dynamics indicating that loss of transition zone proteins alters the basal network activity of *iNeurons*.