# Are “hubs” in beta-cell clusters an emergent network property or do they exist independently?

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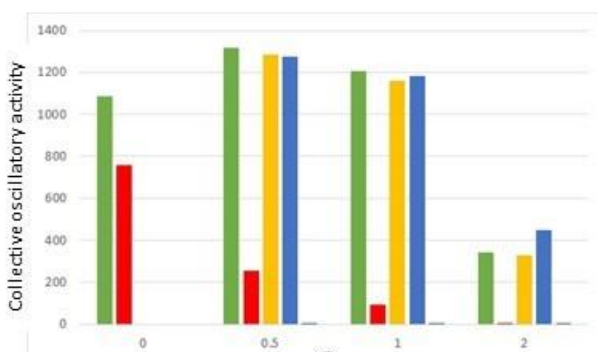
The cell network structure of the pancreatic islets of Langerhans has been the subject of numerous studies. A long-standing dilemma is whether the collective oscillations of beta-cells require the presence of specialized pacemaker cells, named “hubs”, or synchronization occurs through a “democratic” mechanism, where the collective network behavior is a nonlinear average of the properties of its elements. The topic has received so much attention to justify a review focused on the “hub” dilemma [1]. In a recent work [2] we mimicked the architecture of a beta-cell network by a cubic lattice of heterogeneous FitzHugh-Nagumo elements. This topology resembles the experimentally known features of a beta-cell islet. We introduced heterogeneity in the network through a diversified set of external currents Ji, drawn from a Gaussian distribution with standard deviation sigma, which we varied between sigma=0 and sigma=2. Our simulations showed a clear “Diversity-induced resonance”, with a maximum at sigma=0.5, corresponding to a 5% fraction of hubs (the units with Ji corresponding to an intrinsic oscillatory state), in good agreement with experiments [3]. While the above results support the existence of hubs, they do not allow us to decide whether these hubs are an emergent network property or they exist independently of the network. Trying to dig deeper into this, here we present the results of new simulations where we selectively disconnected either hubs or nonhubs from the network. We found rather surprising results, summarized in Fig. 1. We disconnected from the network 1/3 of the hubs, by setting their coupling constant C=0 in the coupled FHN equations. This means the corresponding FHN units had no interaction with other network units. As shown by the red bars in Fig. 1, this caused a dramatic drop of the collective oscillations vs. the reference network configuration, where no elements were disconnected, shown by the green bars. On the other hand, upon disconnecting the same number of nonhubs, we found virtually no change in oscillatory activity, as shown by the yellow bars. This suggests that hubs do play a crucial role as a distinct subset of network elements. However, if we build a truncated distribution of Ji values, where the central range corresponding to oscillatory FHN states is missing, therefore the network is formed by nonhubs only (without any disconnected units), then the global oscillatory activity is also maintained vs. the reference system (blue bars). Therefore, hubs seem to be crucial for global network oscillations if they are initially present and get disconnected, whereas their complete absence does not prevent the network from being in a resonant oscillatory state. In our contribution we will present additional data and hypotheses to explain this apparent contradiction. Our learnings help shed light on the “hub” dilemma but, at the same time, raise new questions that require more work to be fully understood.




References

[1] B.E. Peercy, A.S. Sherman, J. Biosci. 47, 14 (2022).
[2] S. Scialla et al., Phys. Rev. E 103, 052211 (2021).
[3] N. R. Johnston et al., Cell. Metab. 24, 389 (2016).