More is definitely different: the zebrafish as witness: Comment on "Structure and function in artificial, zebrafish and human neural networks" by Peng Ji et al.

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Half a century ago, in his foundation paper *More is different* [1], Anderson stated the relevance of including multiple scales of interaction, instead of trying to reduce everything to fundamental principles. By doing so, one may witness phenomena that were not expected by looking at each individual components separately. This idea finds indeed numerous realizations such as the synchronization phenomenon, where a multitude of dynamical systems suddenly start to behave coherently together, or the spreading of diseases over entire populations, to name only two examples. But if one would have to give a single example of a system where the multiplicity of interaction scales is of utmost importance, it would probably be the *brain*. In their review [2], Ji et al. give a comprehensive overview of the multiple scales of science required in the investigation of structural and functional brain networks, as well as their interplay. Tools borrowed from statistical physics and network theory have been used to reproduce activity patterns observed in measurement data sets and analyze the potential correlation between areas and also neurons. A key issue in the understanding of the neuronal activity and its interplay with the behavior resides in knowing what is the actual dynamics taking place in the brain – e.g. how are the neurons connected together, what are their internal parameters, their input signals. Solving this issue undoubtedly requires the ability to measure the whole-brain activity at the microscopic scale, resolving single neuron dynamics, which is currently not achievable in

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a human brain. However, Ji et al. [2] point out to advances in neuroimaging achieved in the last decade that leaves room for hope in the understanding of brain dynamics for smaller animals such as the *zebrafish*. This comment therefore, focuses primarily on the last part of their review [2], namely the neuroimaging reconstruction of zebrafish networks. As discussed by Ji et al., the zebrafish constitutes an outstanding subject of studies for at least two reasons. First, at its larval stage, the zebrafish has a transparent brain that, together with its small size, makes it very convenient and accessible to recent imaging techniques. Indeed, both the structure and dynamics of the whole-brain neural network can be visualized at single neuron resolution [2]. Second, the zebrafish is capable of a variety of behaviors ranging from prey capture and exploration, to learning and decision making. The latter can be investigated using virtual reality techniques [3], where the fish is placed into predetermined scenarios while its motion is recorded [4]. These two points combined together in the zebrafish provide a unique set-up that enables access to the interplay between neuronal activity and behavioral dynamics, as both can be recorded simultaneously. This promising experimental opening calls for new theoretical developments that include multiple scales of interaction given by the behavior of the fish on one side, and the neuronal dynamics on the other. Relevant related discussions can be found in Ref. [5].

From another perspective, recent research directions have focused on the modelling of the behavior of the zebrafish such as its motion in an environment with obstacles, or its schooling formation. For example, Ref. [6] reproduced its social interactions based on stochastic differential equations where the speed regulation and turning response are incorporated. Recently, Refs. [3, 7] proposed a multi-scale model for the decision making of a juvenile zebrafish that is following other fish. The decision making process about the direction of motion happening in the brain of the fish is modelled by multiple interacting Ising spin systems. The zebrafish then follows this direction with a velocity whose evolution is governed by another stochastic differential equation. Taking one step back, this kind of modelling approach aims not only to reproduce the trajectories of a zebrafish, but rather to emulate the whole interplay between visual input, brain network processing of the information, decision making and motion in an environment. Each part of the process both affects and is affected by the others. A clear advantage of this approach is that it goes beyond looking at the neuronal response to a stimulation. It actually includes the interplay, going back and forth between behavioral response and the neuronal processing.

In the light of the neuroimaging and behavior recording mentioned earlier, such multi-scale approach for the simulation of the zebrafish represents, in my opinion, a first step towards a very promising research avenue. Indeed, high resolution measurements of the neuronal dynamics combined with behavioral experiments could lead to a better understanding of the brain dynamics and thus be used to develop more accurate models able, eventually, to reproduce not only the motion of the zebrafish, but also its associated neuronal activity. Of course, this task is far from being trivial. The microscale structure has to be related to functional networks which themselves must be mapped to specific behaviors. Such a dynamical model would, presumably, if ever, be built step-by-step by adding more layers of complexity, with the guidance of the neuroimaging data, extensively probing the interplay between behavioral response and neuronal activity. While this is a possibly naive point of view of a physicist, such research direction seems promising to me.

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