

Acute Citalopram administration alters zebrafish social dynamics in a behavioral teleporting experiment

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Abstract

In the Star Trek universe, Scotty can “beam you up” and teleport you to a location. Even though science fiction is yet to be reality, is teleporting still possible? Recently, we have developed a robotic platform that is capable of teleporting the behavior of fish from one tank to another through biologically-inspired robotic replicas which map the behavior of a fish from a tank to the other one. Our results indicate that behavioral teleporting is a promising tool to study the biological determinants of behavior. Here we demonstrate its use in pharmacological research, by investigating the effects of selective serotonin reuptake inhibitors of social interactions.

Extended abstract

Zebrafish is an emerging model species in behavioral, pharmacological, and neurological studies (Macrì and Richter, 2015). More and more researchers utilize zebrafish in pre-clinical research to study the underpinnings of anxiety, through pharmacological interventions (de Abreu et al., 2019). Particularly interesting is the use in anxiety-inducing environments of selective serotonin reuptake inhibitors, such as Citalopram, which is commonly used to treat anxiety in humans (Karakaya et al., 2020b). However, it has been heretofore difficult to unravel the specific effects on social behavior of these pharmacological, as drug administration is accompanied by changes in color of zebrafish and olfactory cues that confound the interaction between the animals. To overcome this limitation, we propose to use biologically-inspired robots that can mimic the behavior of live fish.

This idea builds upon previous efforts in the literature aimed at interfacing the ethograms of animals in different locations. Bonnet *et al.* (Bonnet et al., 2019) introduced a robotic platform that allows for interactions between groups of two different species (zebrafish and bees) that are located in two remote locations. Larsch and Baier (Larsch and Baier, 2018) established a virtual reality platform that allows for interactions between two larval zebrafish in separate locations. Taking inspiration from these works, we developed the novel experimental paradigm of “behavioral teleporting”, which consists of two robotic platforms controlled in real-time (Fig. 1) (Karakaya et al., 2020a). Within

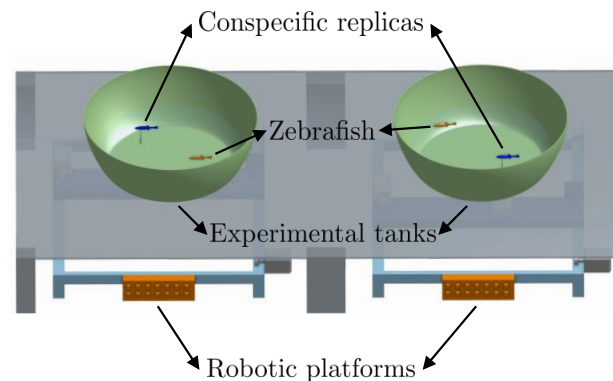


Figure 1: Schematic of the behavioral teleporting setup. Robotic platforms are positioned under two experimental tanks, each containing a live fish and a replica. Both the fish and the replicas are tracked in real-time using overhead webcams. Real fish are shown in yellow, and robotic replicas in blue.

this paradigm fish 1 interacts with replica 1 that mimics the behavior of fish 2 that is swimming in a different tank. Fish 2, in turn, interacts with replica 2 that is mirroring the behavior of fish 1 (Fig. 2a). Just like the title of the conference, our robots come ALIVE in real-time and enable interactions with animals.

Our interactive robots show how artificial life can engage with live animals. Through behavioral teleporting, we eliminate the need for a mathematical framework that guides the underlying behavior of the robots. Instead we allow for the behavior of live animals to be transferred onto robots in real-time. This biologically-inspired system can be used to understand the underpinning of social behavior, which paves the way for better artificial systems. The strong coupling between real and artificial life shown in the behavioral teleporting is of importance to ALIFE.

Utilizing the behavioral teleporting setup, we seek to understand the effects of anxiety on social behavior. Towards this aim, we treat fish with different concentrations of

Citalopram (0 mg/L, 30 mg/L, and 100 mg/L). We test pairs of treated fish in our experimental platform, performing experiments on all the six possible combinations of treatments (Fig. 2b). Each fish is exposed to Citalopram in a beaker for 5 minutes prior to the beginning of a trial, before being gently hand-netted into the experimental tanks and allowed to habituate for 5 minutes in an opaque cylinder. At the end of the habituation period, the robotic platforms are initialized, and behavioral teleporting is started. Fish and replicas are tracked in real-time through an in-house built software. Behavioral metrics are extracted from the trajectory data of the animals.

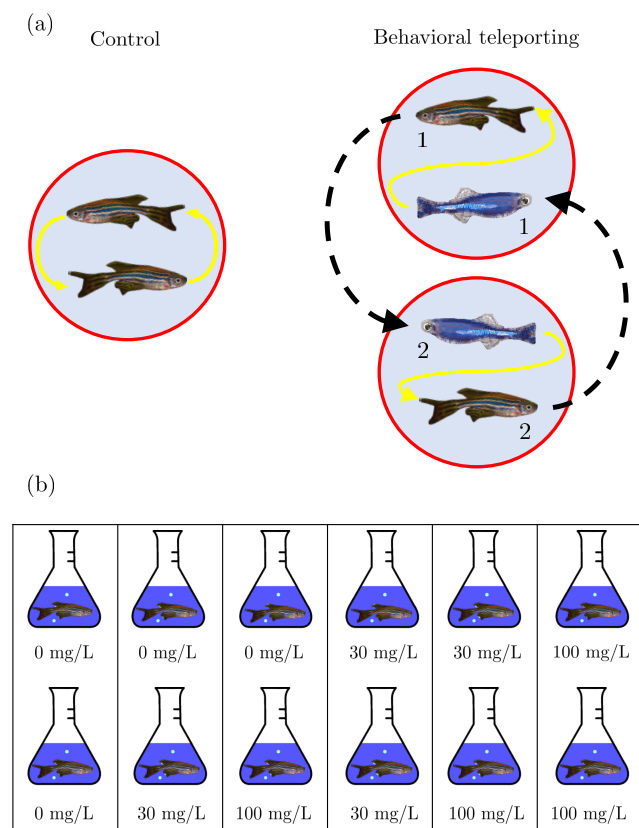


Figure 2: Experimental conditions for behavioral teleporting. (a) We studied a “control” condition where two fish treated with 0 mg/L Citalopram swam in the same tank, and six “behavioral teleporting” conditions where two live fish treated with different concentrations of Citalopram swam in separate tanks alongside robotic replicas. Solid yellow lines show direct interaction, and dashed red lines depict behavioral teleporting. (b) Citalopram treatments for the fish in the “behavioral teleporting” conditions: each column indicates a combination of Citalopram concentration administered to the live fish.

In this work, we plan to test the following hypotheses:

- When fish are treated at two different Citalopram concentrations, two-way interaction between the animals should emerge with one of the animals taking the role of the leader.
- When fish are treated at the same Citalopram concentration, a concentration dependent two-way interaction should emerge, without signs of leaderships.

In our previous effort (Karakaya et al., 2020a), we showed that behavioral teleporting was successful in preserving the interactions between two live animals located in separate tanks. Cross-correlation and transfer entropy analysis indicated that there was a two-way interaction between the live animals, and when the conspecific replicas were the same size of the fish they were mirroring, small fish emerged as the leaders as in the corresponding control condition. A further analysis on social behavior metrics, such as inter-individual distance and polarization, showed that the robotic replicas might induce a state of anxiety. Here, we expect acute Citalopram administration to strengthen the interaction between live animals facilitated through behavioral teleporting due to a reduction in anxiety levels. Pilot trials indicate that inter-individual distance is reduced and polarization is increased when both fish are administered 30 mg/L of Citalopram in comparison to 0 mg/L.

Behavioral teleporting allows fine control of morphophysiological and behavioral traits toward the systematic analysis of the determinants of social behavior. Through the experiments presented herein, we plan to demonstrate the use of behavioral teleporting for pharmacological studies.

Acknowledgements

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References

- Bonnet, F., Mills, R., Szopek, M., Schönwetter-Fuchs, S., Halloy, J., Bogdan, S., Correia, L., Mondada, F., and Schmickl, T. (2019). Robots mediating interactions between animals for interspecies collective behaviors. *Science Robotics*, 4(28).
- de Abreu, M. S., Giacomini, A. C., Genario, R., Dos Santos, B. E., da Rosa, L. G., Demin, K. A., Wappler-Guzzetta, E. A., and Kalueff, A. V. (2019). Neuropharmacology, pharmacogenetics and pharmacogenomics of aggression: The zebrafish model. *Pharmacological Research*, 141:602–608.
- Karakaya, M., Macrì, S., and Porfiri, M. (2020a). Behavioral teleporting of individual ethograms onto inanimate robots: experiments on social interactions in live zebrafish. *iScience*, 23(8):101418.

- Karakaya, M., Scaramuzzi, A., Macrì, S., and Porfiri, M. (2020b). Acute citalopram administration modulates anxiety in response to the context associated with a robotic stimulus in zebrafish. *Progress in Neuro-Psychopharmacology and Biological Psychiatry*, page 110172.
- Larsch, J. and Baier, H. (2018). Biological motion as an innate perceptual mechanism driving social affiliation. *Current Biology*, 28(22):3523–3532.
- Macrì, S. and Richter, S. H. (2015). The snark was a boojum-reloaded. *Frontiers in Zoology*, 12(1):1–13.