Computational model-based analysis of spatial navigation strategies under stress and uncertainty using place, distance and border cells

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BACKGROUND

Stress facilitates learning & memory…

Or does it?

It depends on the type of learning & memory.

Importantly, also on what we exactly mean by it!

Decision-making occurs during navigation and learning. It is widely studied in choice behaviors, but less well understood in natural and more continuous settings, especially under **stress** and **uncertainty**. This process could be investigated in **rodent spatial navigation**, which has been modeled with place-cell-based models. However, traditional models usually ignored **detailed trajectories or kinematics**. Here we extended a **place cell-based reinforcement learning model** to include detailed kinematics and used it to investigate the role of motivational stress in **Morris Water Maze**. We performed experiments with two strains of mice learning two versions of the task under different **water temperatures**: the task with a fixed platform location and the task where platform location varied randomly between two positions. Using **computational modeling** and **parameter estimation**, we were able to not only reproduce detailed mouse behaviors but also reveal computational correlates of **temperature-based behavioral differences**. Our findings provide insights into computational mechanisms underlying spatial navigation in mice and how various modulators influence it.

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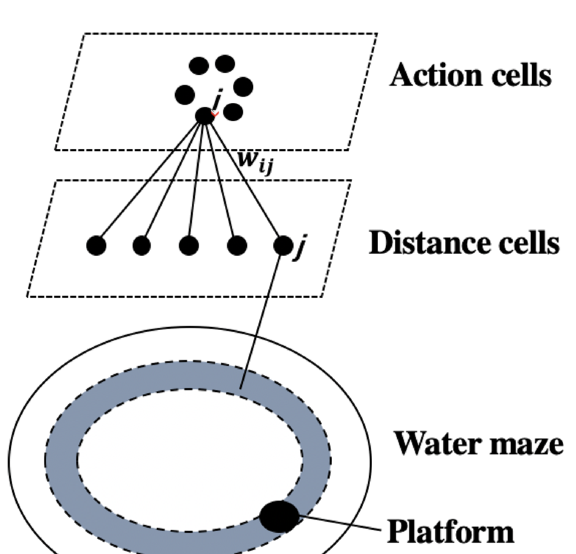
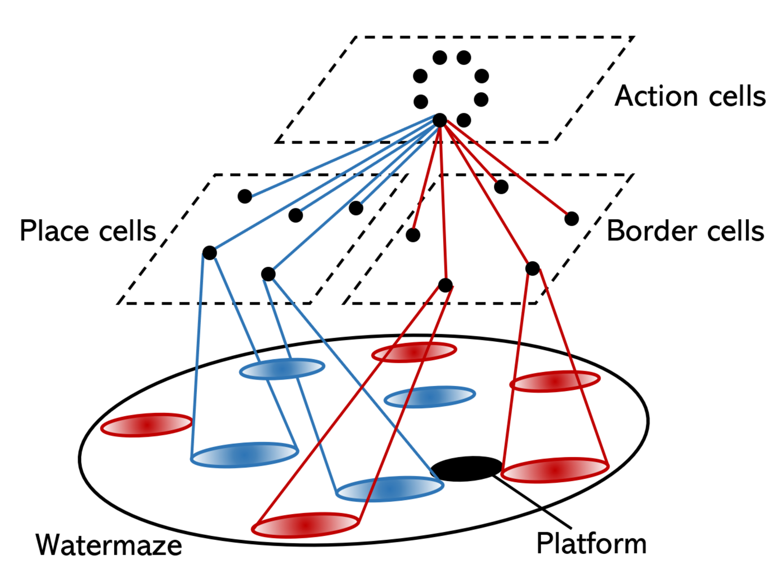
MODEL EXTENSIONS



We then extended the model to include a wall-distance-based component, where spatial learning would be guided not just by place information but also by a cue-like signal, namely distance to the wall, which reproduced mouse behavior in tasks with uncertain platform positions better than place-cell-based strategies alone.

$$r_j^{dc} = \exp(-(d-d_j)^2/2\sigma_{dc}^2)$$



Based on that, we further implemented a more biologically plausible model that uses a combination of border (boundary) cells and place cells.
The border cells are the cells with receptive fields distributed close to the border of water maze. They are sensitive to the distance to the wall like DCs, but they have definite location of receptive field.

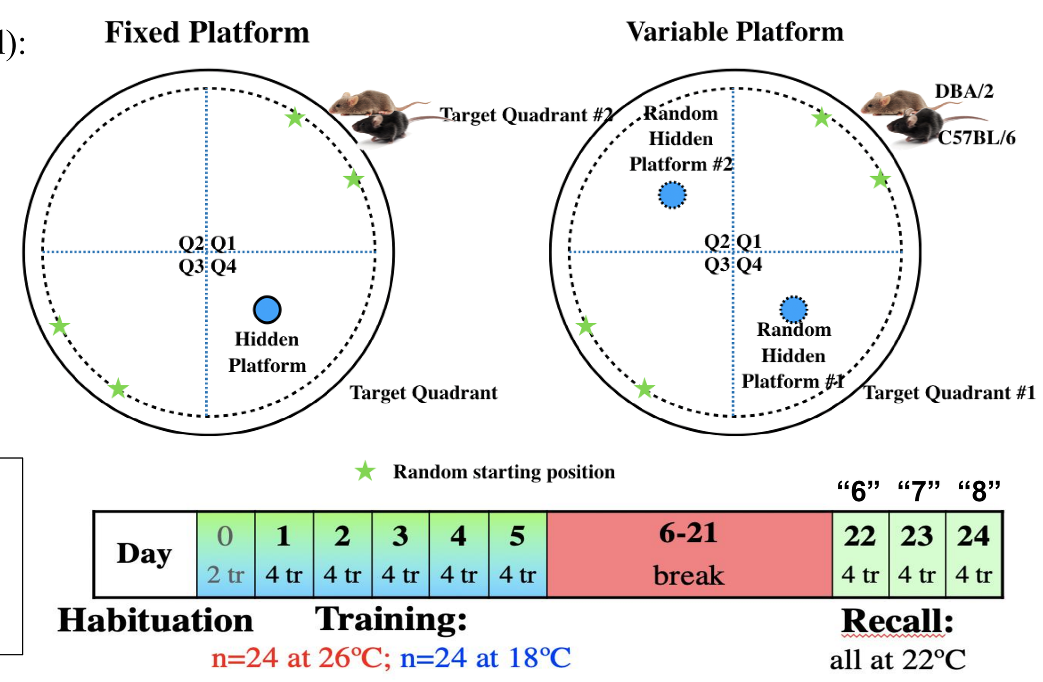
$$r_j^{bc} = \exp\left(-\frac{|d-d_j|^2}{2\sigma_{d_{bc}}^2}\right) \times \exp\left(-\frac{|\theta-\theta_j|^2}{2\sigma_{\theta_{bc}}^2}\right)$$

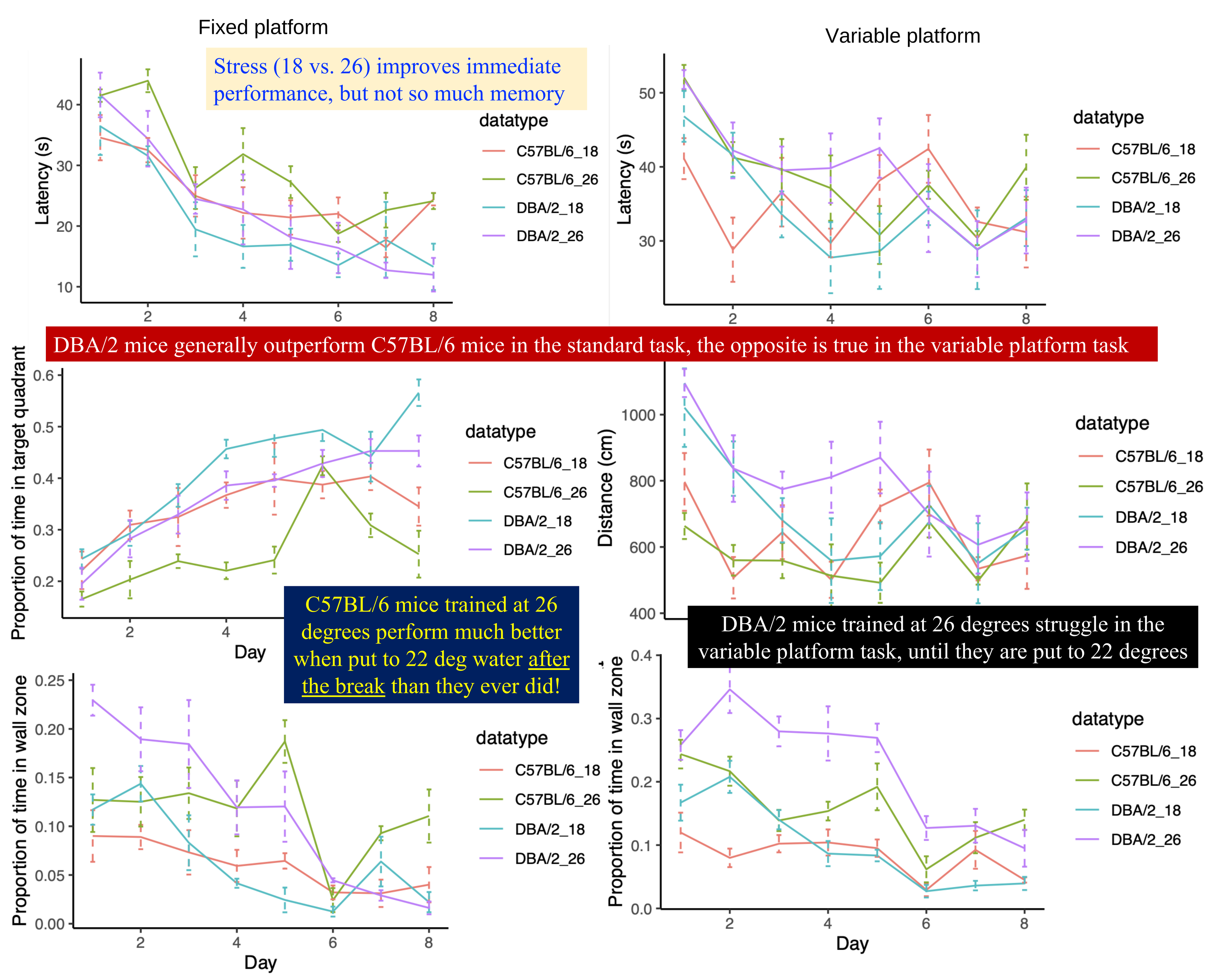
EXPERIMENTAL DESIGN AND BEHAVIORAL RESULTS

Performance measures (PM) (for each mouse and trial):

- Swim distance (m)
- Latency to platform (s)
- Swim speed (m/s)
- Time %-s in the target quadrant, opposite quadrant, (or combined target + opposite quadrants in variable platform task) and the wall zone
- Mean turning angle

How do genetic strain, immediate temperature and previous temperature influence performance based on different measures?



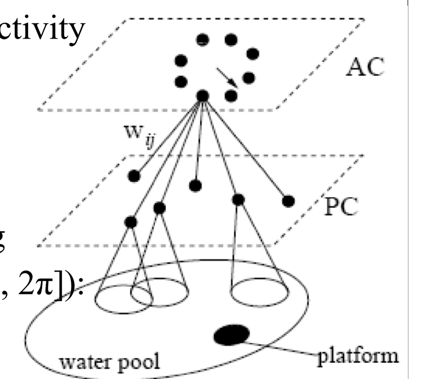


PLACE CELL-BASED MODEL

The position of the animal *(state s(t))* is represented as a population activity of **'place cells'** (PC):

$$r_j^{pc} = \exp(-\|\vec{p}-\vec{p}_j\|^2/2\sigma_{pc}^2)$$

PCs project to a population of **'action cells'** (AC, representing directions of movement φ_i in $[0, 2\pi]$):



$$Q(s_t, a_t) = r_i^{ac} = \sum_j w_{ij} r_j^{pc}$$

Weights w_{ij} are initialized as uniformly distributed randoms from $[0, W_{mult}]$ and decay at a rate W_{dec} at each time step.

Weights are updated as to <u>decrease the reward prediction error δ</u>: $\delta = Reward(t) + \gamma Q_{t+1} - Q_t$, where γ is temporal reward discounting factor.

Action choice: matching law with exploitation factor β (=„log softmax")

$$p(a|s) = Q(s,a)^\beta \Big/ \sum_{a_i \in A(s)} Q(s,a_i)^\beta$$

Eligibility trace keeps a (decaying) record of performed actions $e_{ij} = \lambda e_{ij} + r_i^{ac'} r_j^{pc}$, where λ is the eligibility trace decay rate.

Finally, weights are updated as follows: $\Delta w_{ij} = \alpha\, \delta\, e_{ij}$, where α is the learning rate.

In order to simulate realistic trajectories, acceleration (ac_const) is added at each step in the direction of the selected action. In addition, the existing velocity decays at each time step with multiplying it by V_{decay}.

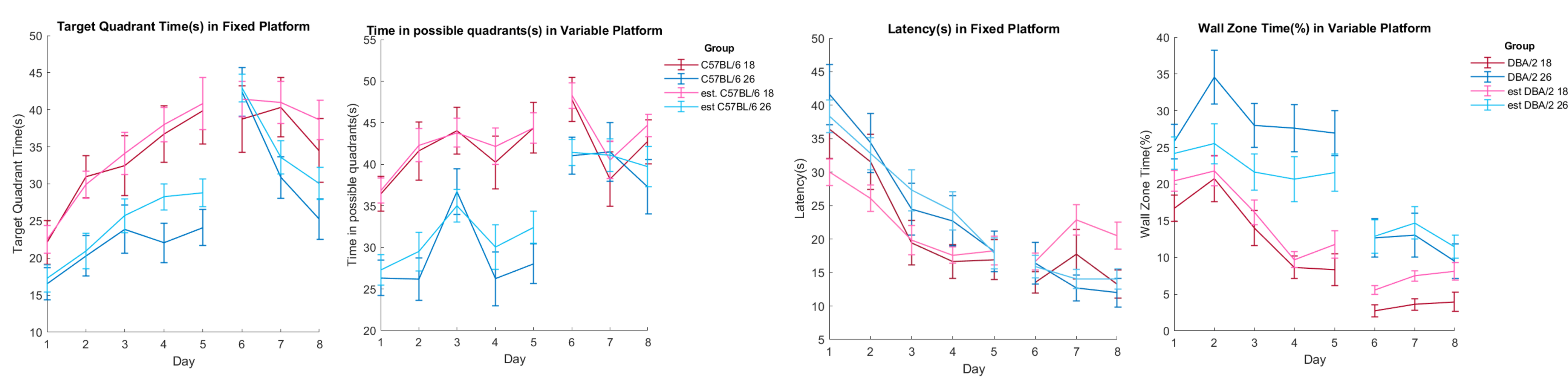
Higher ac_const values represent more vigorous push in the selected direction. Higher V_{decay} values suggest more inertia in movement and more difficulty to change directions, which may especially be needed during the search around the platform. Once the modeled mouse hits the wall, the normal component is reset to 0, but the tangential component is preserved.

$$(v_x, v_y) = \Big((v_x, v_y) + ac\_const(\cos((\varphi_{sel})), \sin((\varphi_{sel})))\Big) v_{decay}$$

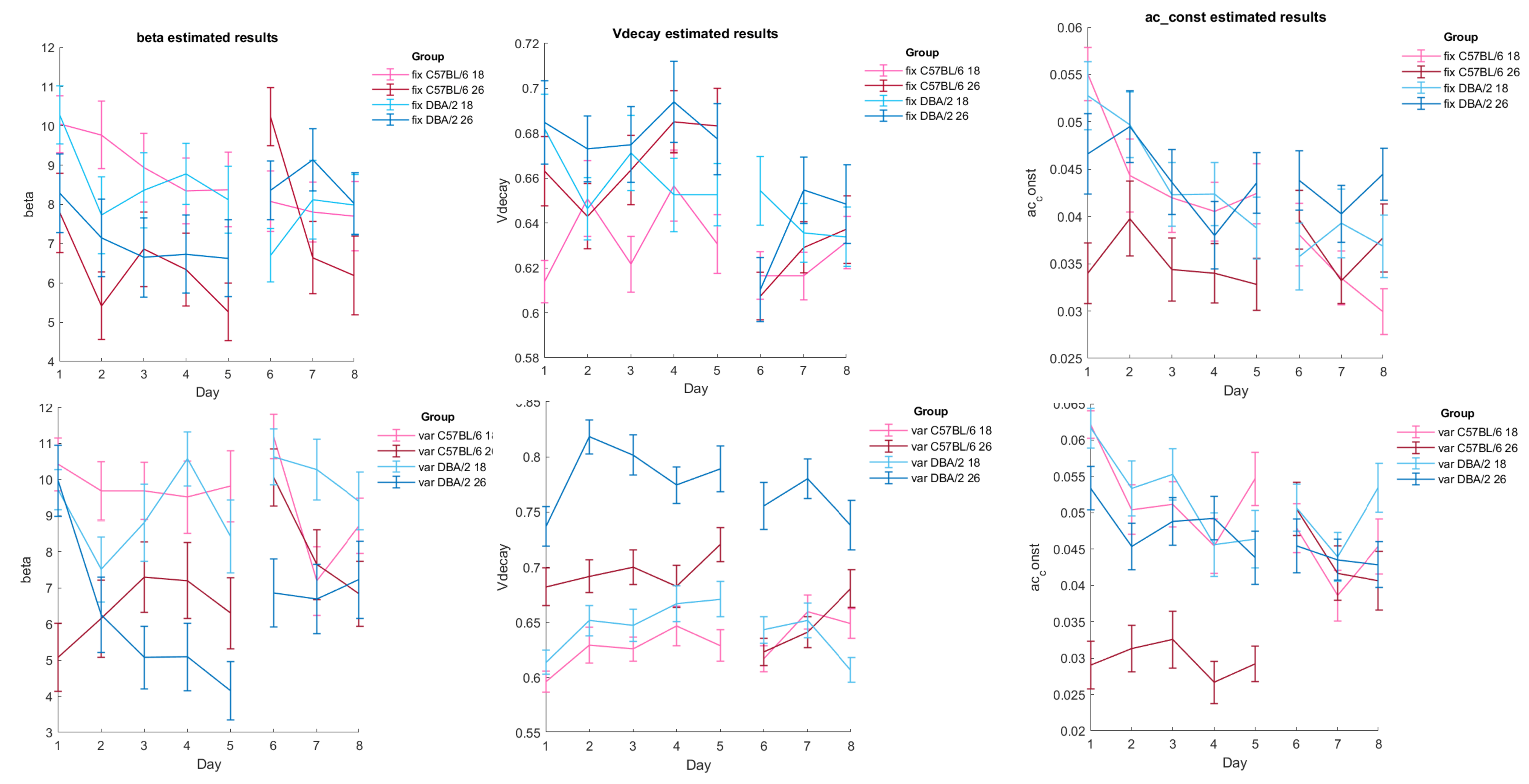
Acceleration is applied in the chosen direction and velocity decays with time based on acceleration. Then, movement is computed based on current velocity.

PARAMETER ESTIMATION

We estimated best-fitting parameters of models with place and border cells in different experimental conditions and genetic strains of mice. First, we selected the least sensitive parameters to be fixed across days/conditions, as all cannot be flexible: **among them, crucially, the learning rate.**



The achieved fits were good to excellent, reproducing differences in different variables between groups



MODEL-DERIVED INTERPRETATION

- Across tasks and strains, **cold water consistently leads to increased exploitation of knowledge** (higher beta). These differences mostly disappear once the mice are put to 22 deg water after the break.
- DBA/2 mice performing the variable platform task in warm water have **considerably higher inertia** of their movement (high Vdecay), likely explaining their poor performance and high thigmotaxis in 26 deg water.
- **C57BL/6 mice** learning in **warm** water have considerably **lower acceleration constants** than other groups, suggesting that their performance vigour is reduced. This disappears when put to 22 deg water.
- YES, **cold water stress improves learning,** but mostly by **modulating exploration-exploitation balance and performance vigour**, not the learning rate per se. This **may lead** to somewhat **more solid memory representations**, but **immediate effects are much stronger than long-term effects**!

REFERENCE: Luksys, Gerstner & Sandi, *Nat. Neurosci.* 2009