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Hierarchical Inference: PET and sMRI

We infer a coupled model of FKPP and atrophy:

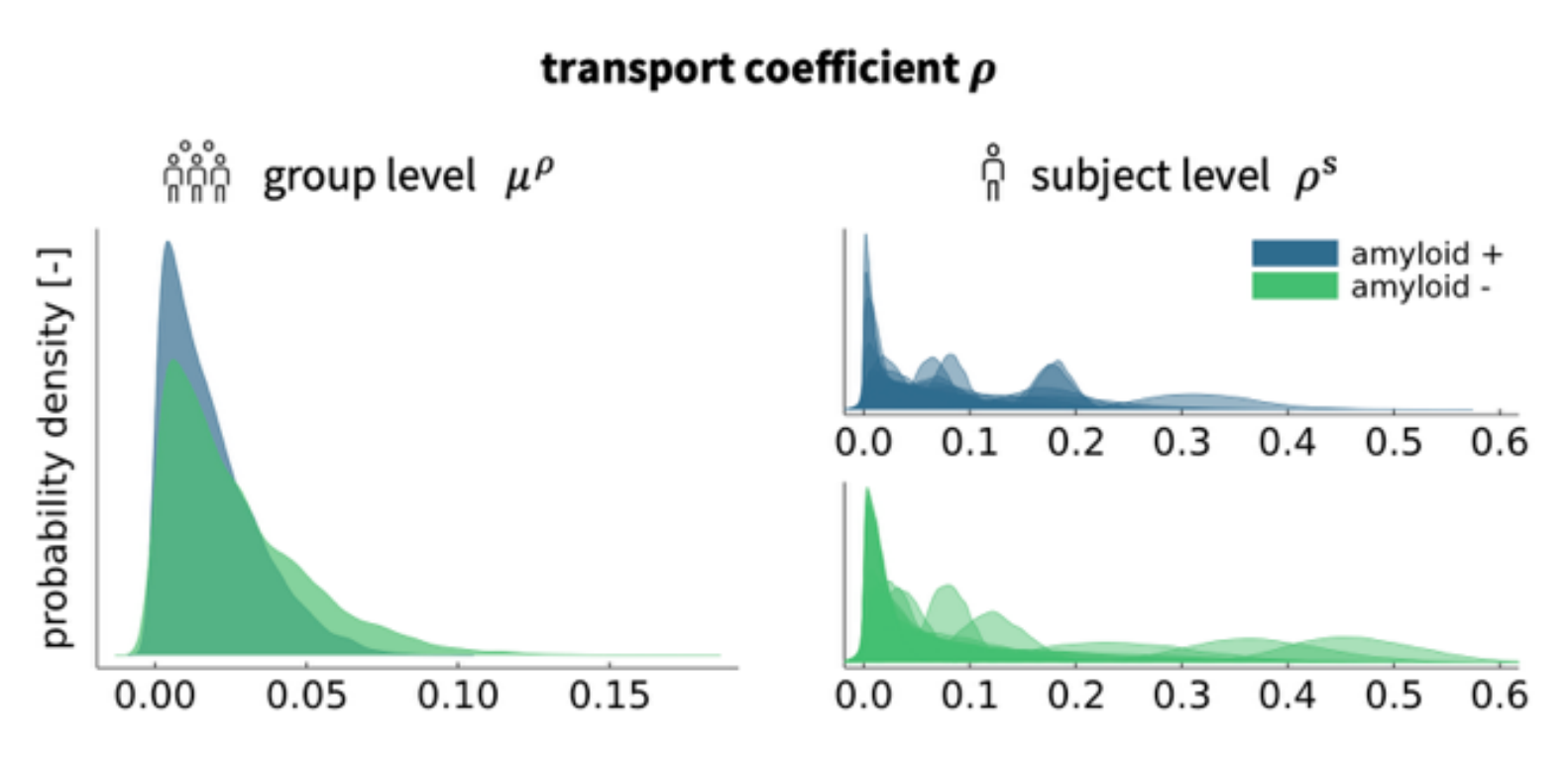
$$\frac{dc_i}{dt} = -\rho \sum_{j=1}^{N} L_{ij}c_i + \alpha c_i(1 - c_i)$$
$$\frac{\mathrm{d}q_i}{\mathrm{d}t} = G_c c_i(1 - q_i)$$

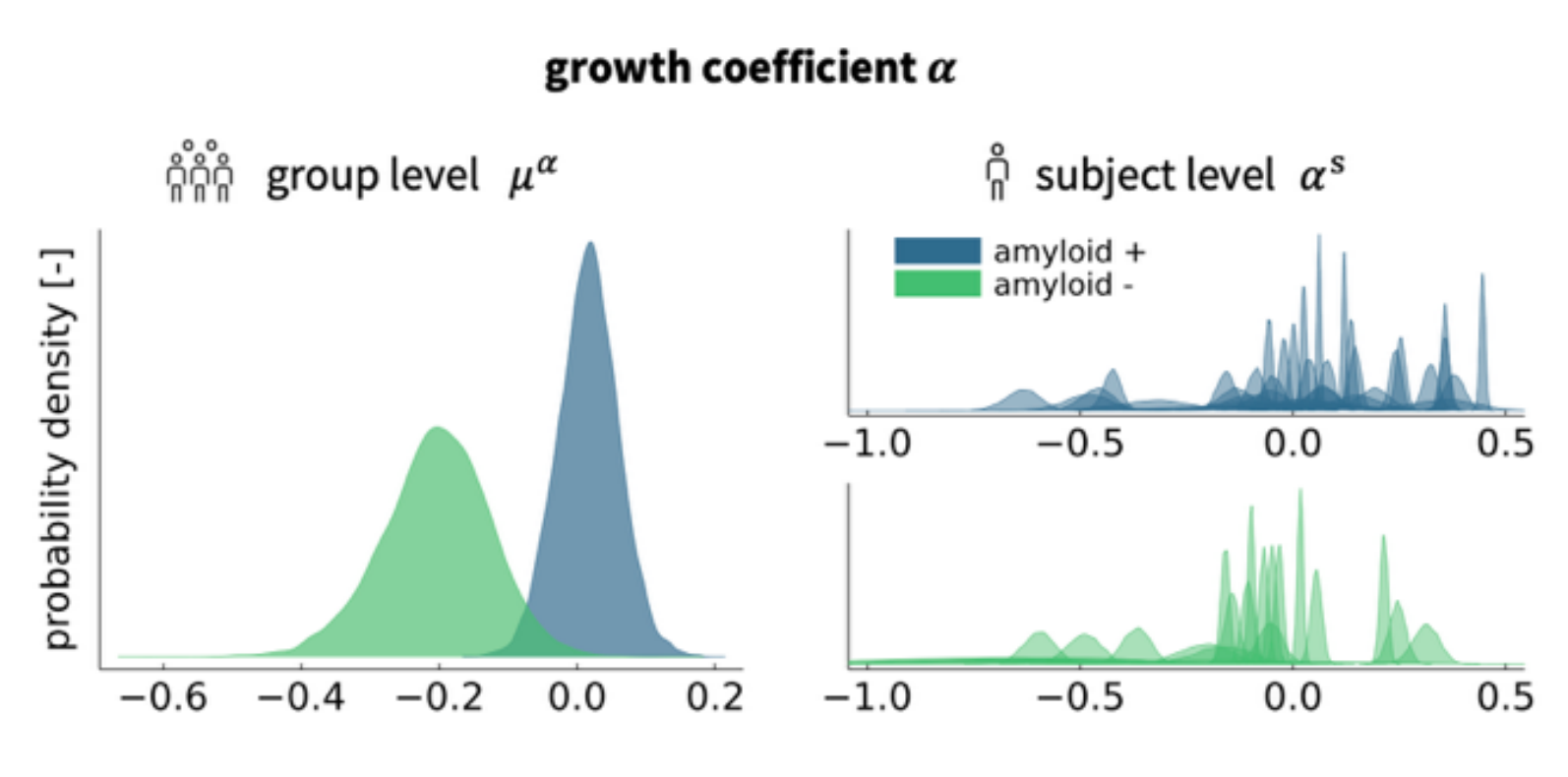
Inference Results

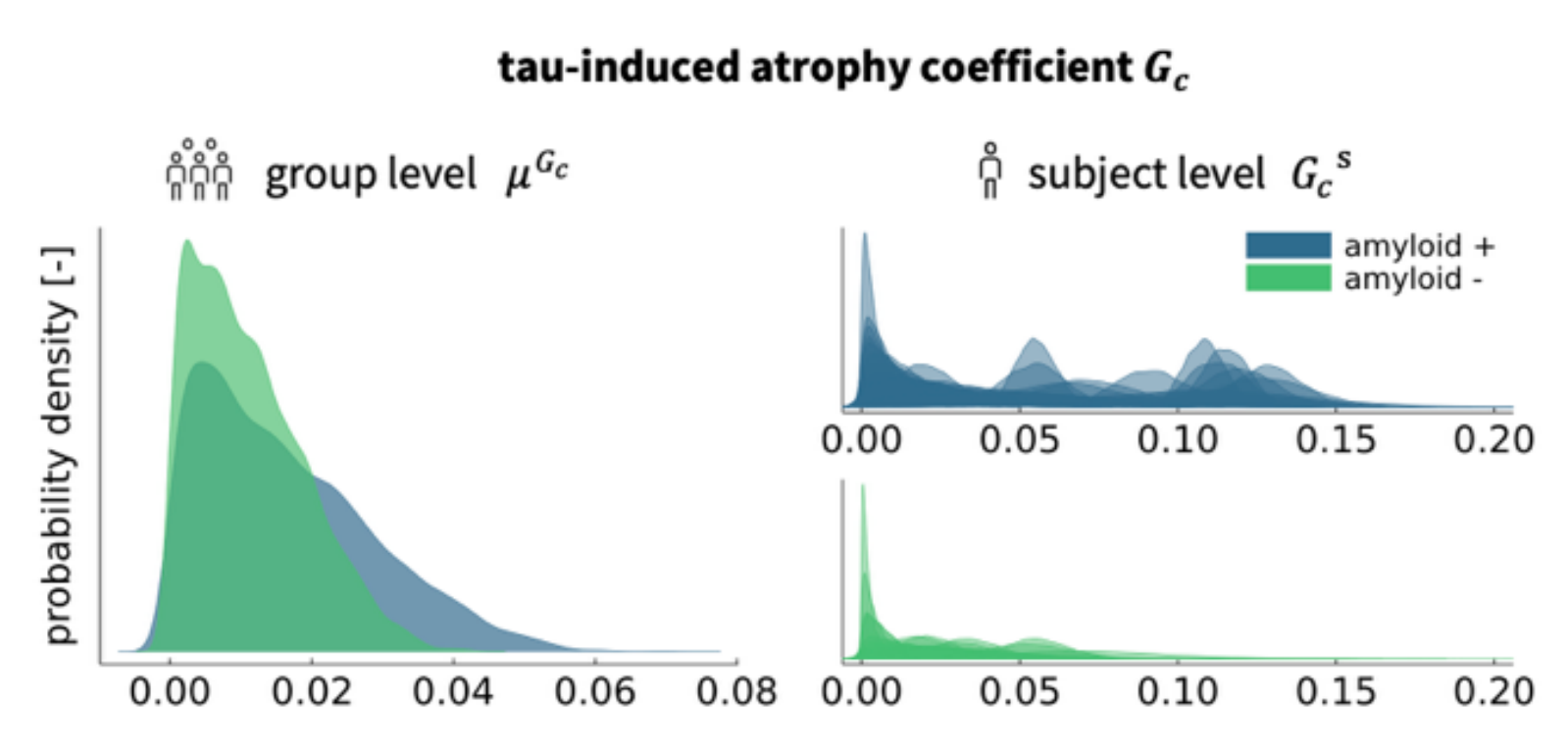
We use hierarchical priors on all model parameters, ρ, α, G_c. We have the following model structure:

$$\begin{aligned}
\sigma_t &\sim \Gamma^{-1}(2,3) \\
\sigma_a &\sim \Gamma^{-1}(2,3) \\[1em]
\rho_\mu &\sim \mathcal{N}^{+}(0,1) \\
\rho_\sigma &\sim \mathcal{N}^{+}(0,1) \\[1em]
\alpha_\mu &\sim \mathcal{N}(0,1) \\
\alpha_\sigma &\sim \mathcal{N}^{+}(0,1) \\[1em]
\beta_\mu &\sim \mathcal{N}^{+}(0,1) \\
\beta_\sigma &\sim \mathcal{N}^{+}(0,1) \\[1em]
\rho_i &\sim \mathcal{N}^{+}(\rho_\mu, \rho_\sigma) \\
\alpha_i &\sim \mathcal{N}(\alpha_\mu, \alpha_\sigma) \\
\beta_i &\sim \mathcal{N}^{+}(\beta_\mu, \beta_\sigma) \\[1em]
y_i^{tau} &\sim \mathcal{N}(f(\mathbf{u}, t, \{\rho_i, \alpha_i, \beta_i\}), \sigma_t) \\
y_i^{atr} &\sim \mathcal{N}(f(\mathbf{u}, t, \{\rho_i, \alpha_i, \beta_i\}), \sigma_a)
\end{aligned}$$

for $i \in 1 \dots N$ subjects. Notice that we assume the same noise distribution across all subjects. Initial tests with independent noise for each subject showed poor convergence. Identical noise for each subjects does not account for subject movement in scanners or differences in scanner hardware and protocols. The hierarchical distributions for transport and growth are consistent with those reported in previous studies. There are clear differences in the hierarchical distributions for atrophy between the AB+ groups and the AB- groups, with the latter having a lower density around smaller values and a wider tail. This is reflected in the subject-specific distributions, which show a significantly greater portion of posterior distributions away from 0 for AB+ compared to Ab-.







Inferring Seeding Locations

Problems:

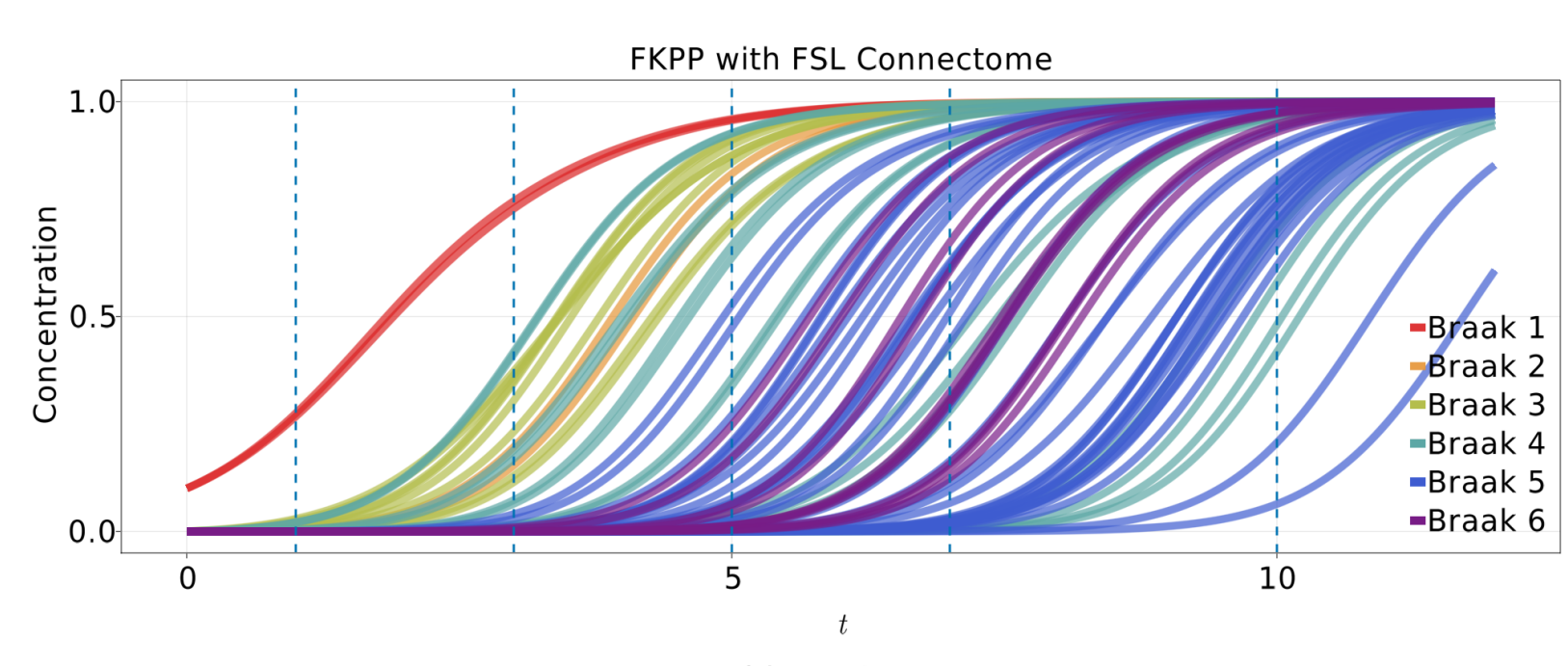
- Given some data from $t_n = t_{0+n}$, can we infer initial conditions at $t = t_0$?
- Does parameter identifiability vary given connectome topology?

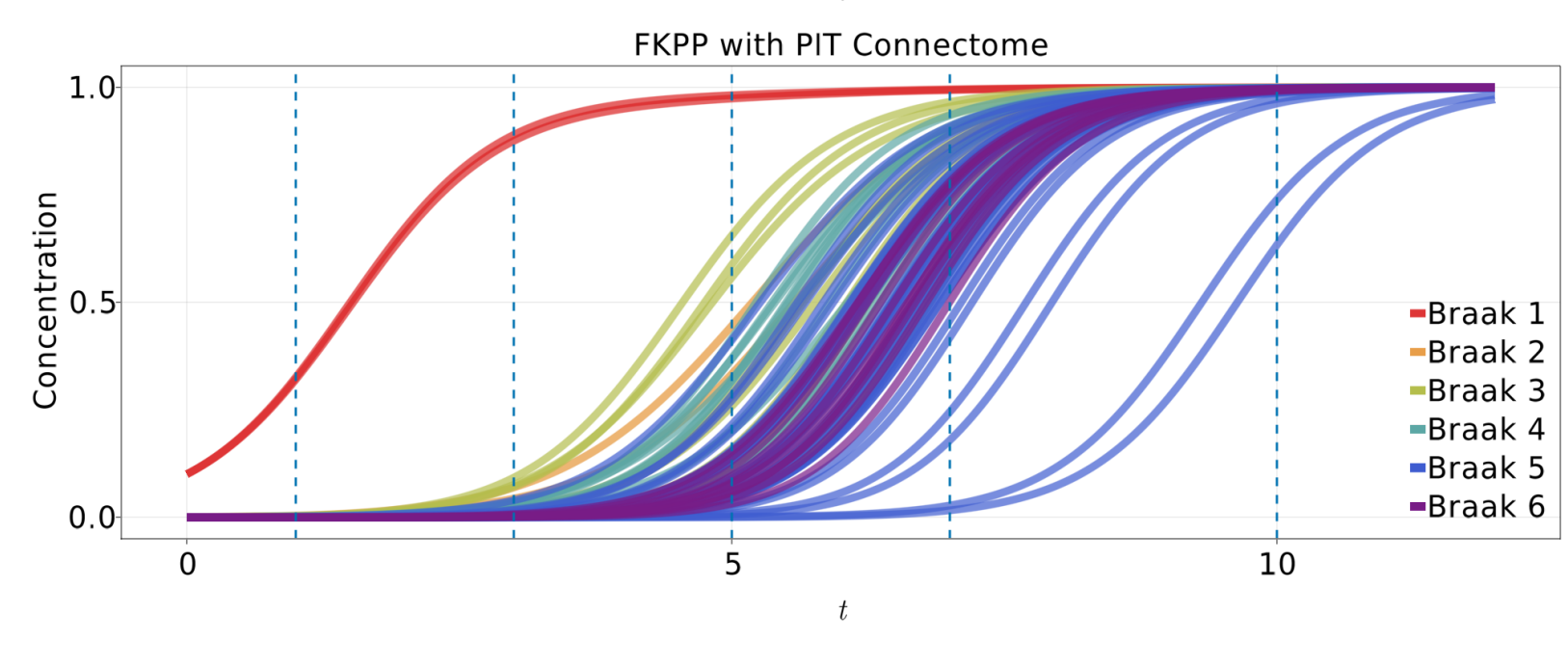
I first explore identification of 10% seeding in bilateral EC. Synthetic data is generated using FKPP simulations on the FSL and PIT connectomes, with parameters $\rho = 0.5$ and $\alpha = 1.5$. I test 5 time intervals for $n \in \{1, 3, 5, 7, 10\}$, shown by the dashed lines. For each n, FKPP solutions at each node are saved at t_n, t_{n+1} and t_{n+2}, giving 83×3 data points per test case.

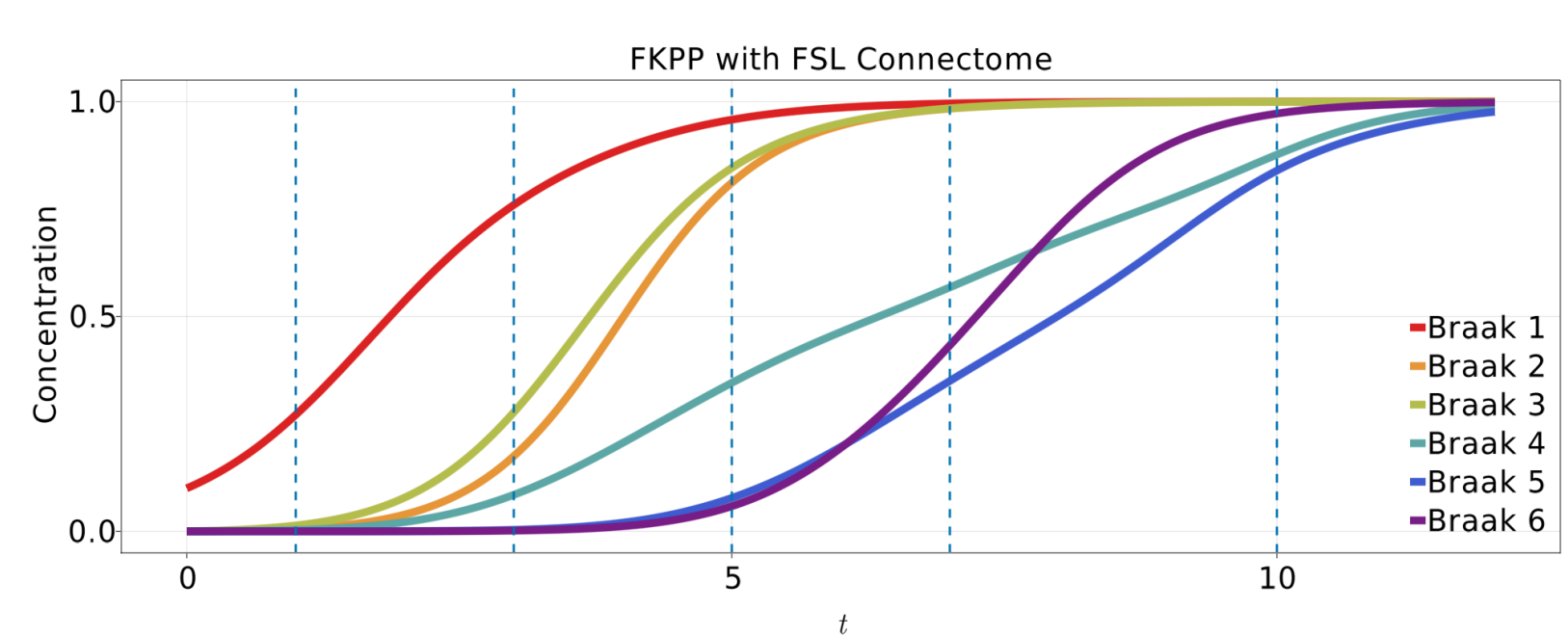
Additionally, for each value of n, we test identifiability at 4 noise levels, given by:

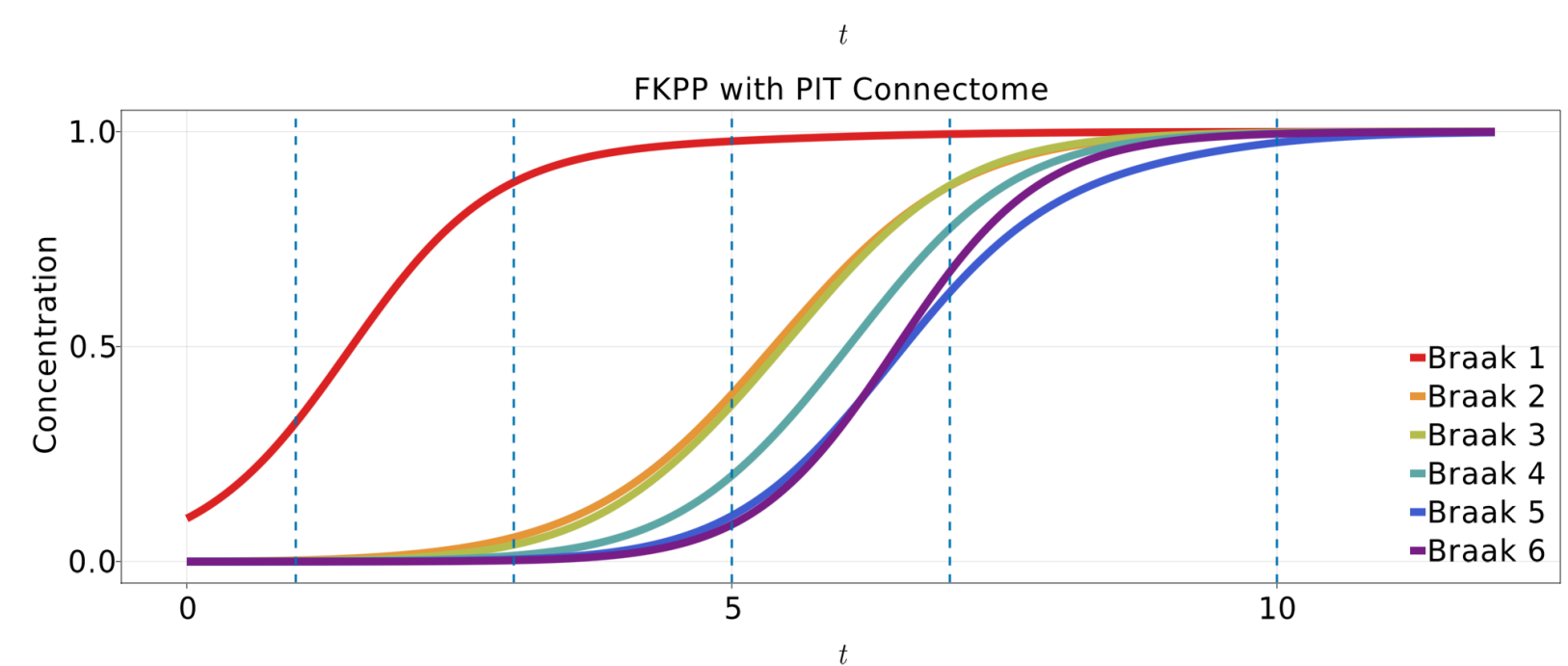
$$y = f(\mathbf{u}, t, \mathbf{p}) + \mathcal{N}(0, \sigma)$$

for $\sigma \in \{0, 0.02, 0.05, 0.1\}$.









Inference Model

I use a horseshoe prior to enforce sparsity in solutions to the inference problem. The full generative process is then defined as:

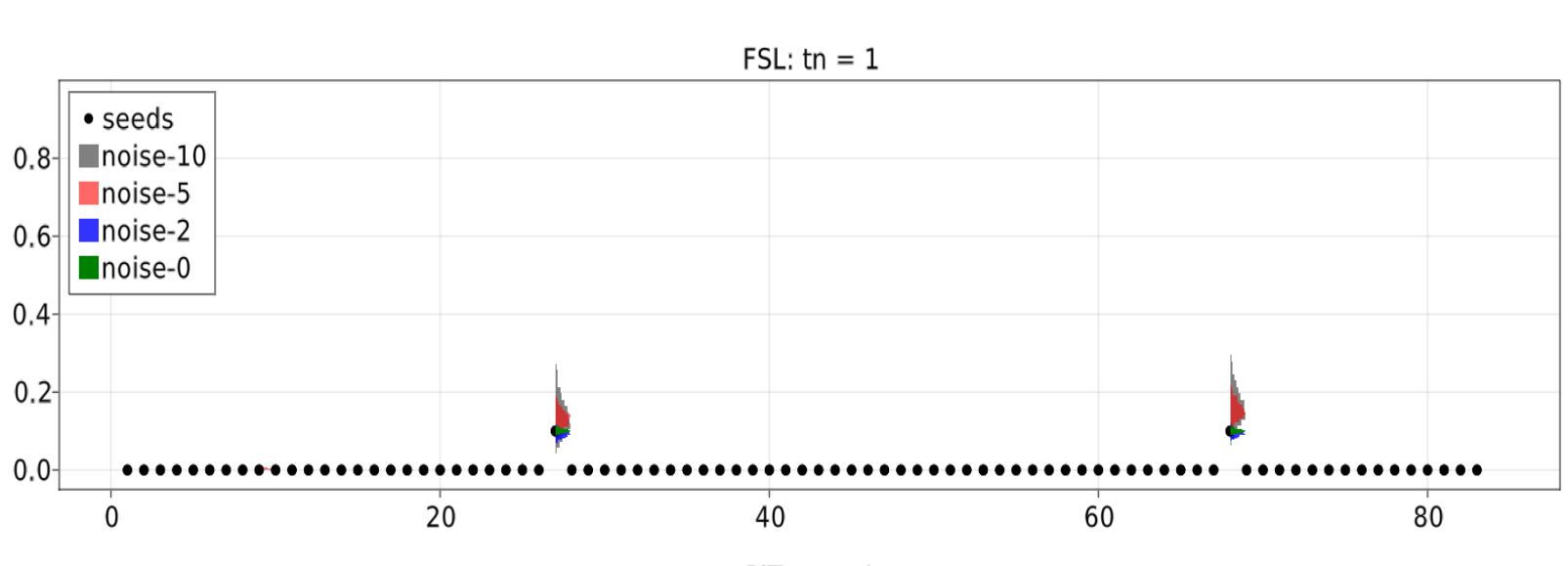
$$\begin{aligned}
\sigma &\sim \Gamma^{-1}(2,3) \\[1em]
\tau &\sim \mathcal{C}^{+}(0, 0.1) \\
\lambda_i &\sim \mathcal{C}^{+}(0, 1) \\
\omega_i &\sim \mathcal{N}(0, 1, [0, 1]) \\[1em]
\rho &\sim \mathcal{N}^{+}(0,1) \\
\alpha &\sim \mathcal{N}^{+}(0,1) \\[1em]
u_i &= \omega_i * (\tau * \lambda_i) \\
y &\sim \mathcal{N}(\mathbf{f}(\mathbf{u}, t, \theta)|_{t_{0+n}}, \sigma)
\end{aligned}$$

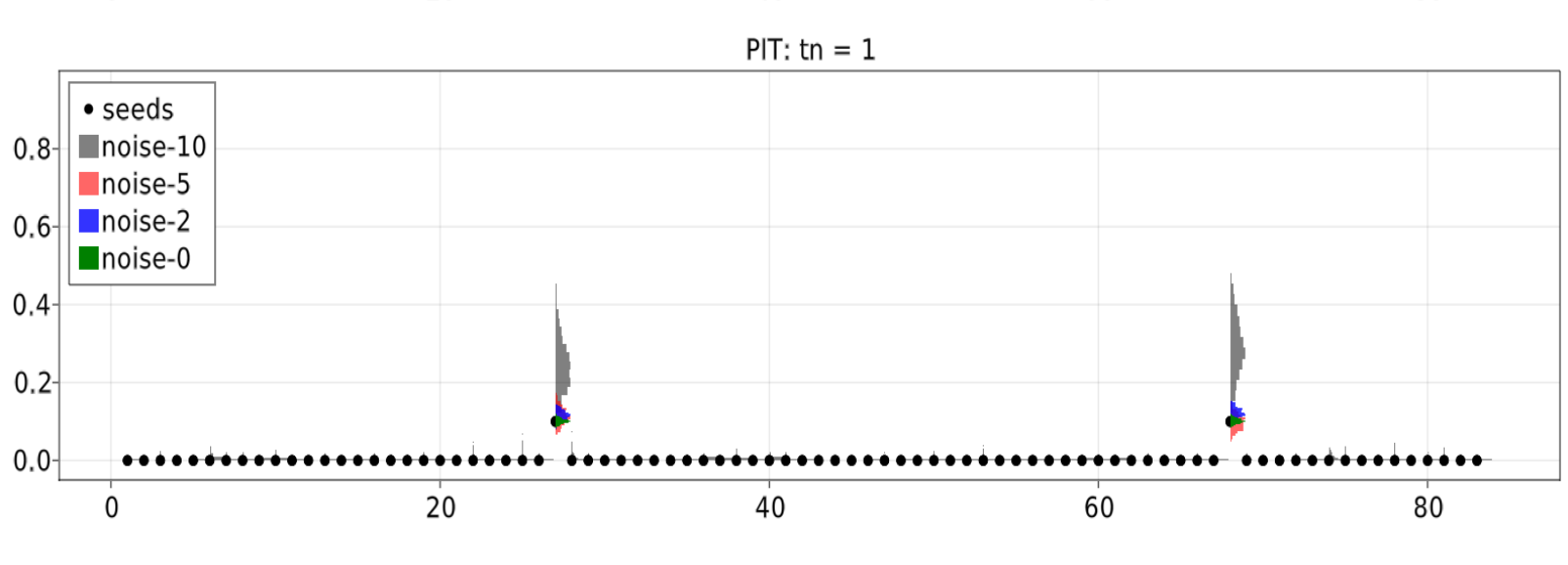
Inference Results

Entorhinal Seeding

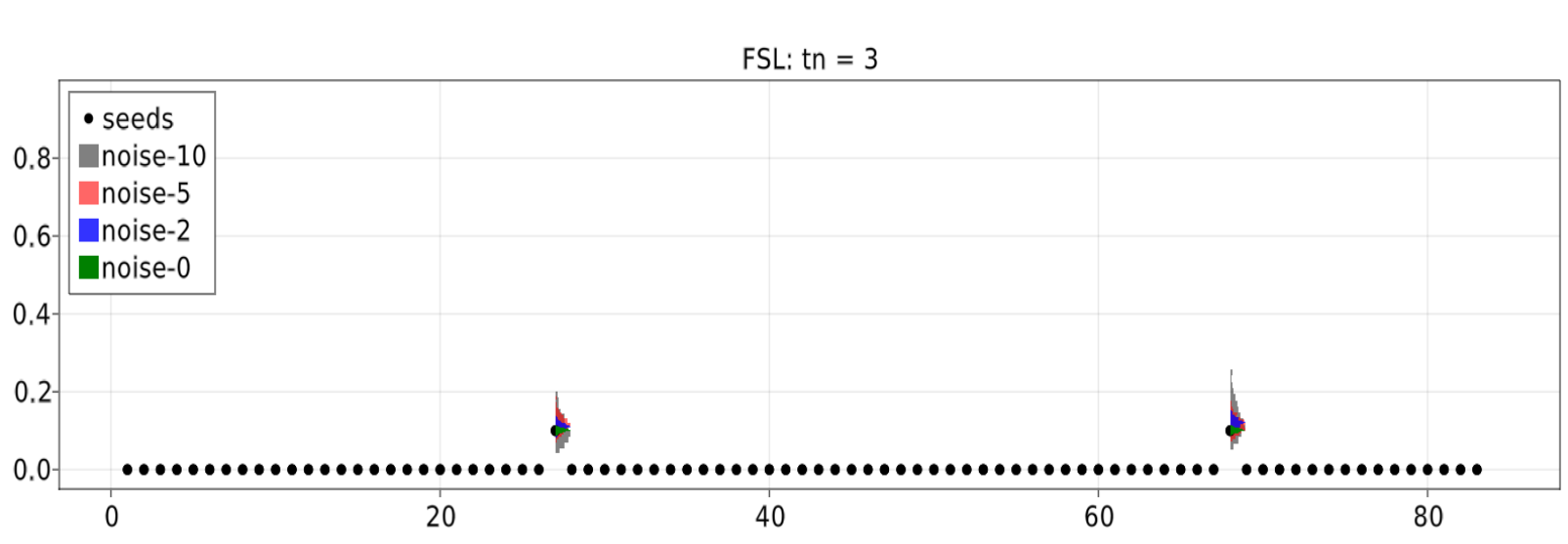
$t_{n=1}$

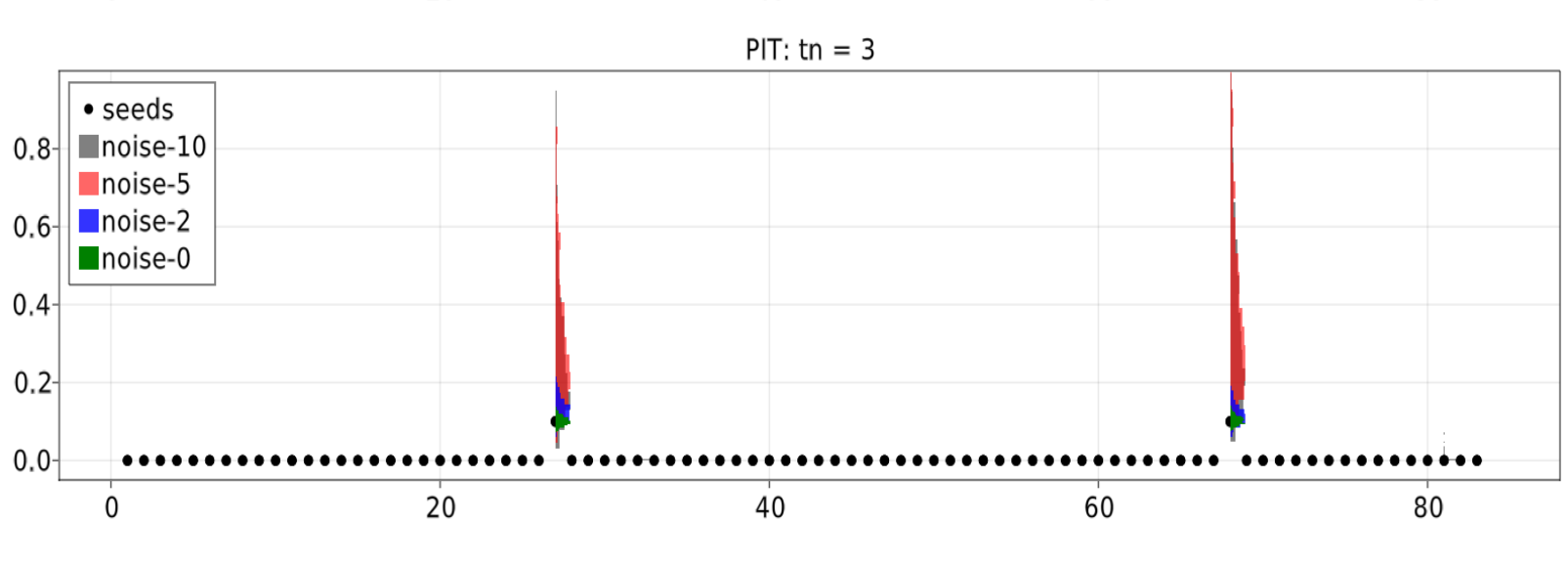
For $n = 1$ and $n = 3$, the locations of the initial conditions are identified for all noise levels using the FSL and PIT connectomes. However, in both cases, posteriors are broader for the PIT connectome than the FSL connectome at higher noise levels (0.05 and 0.1).





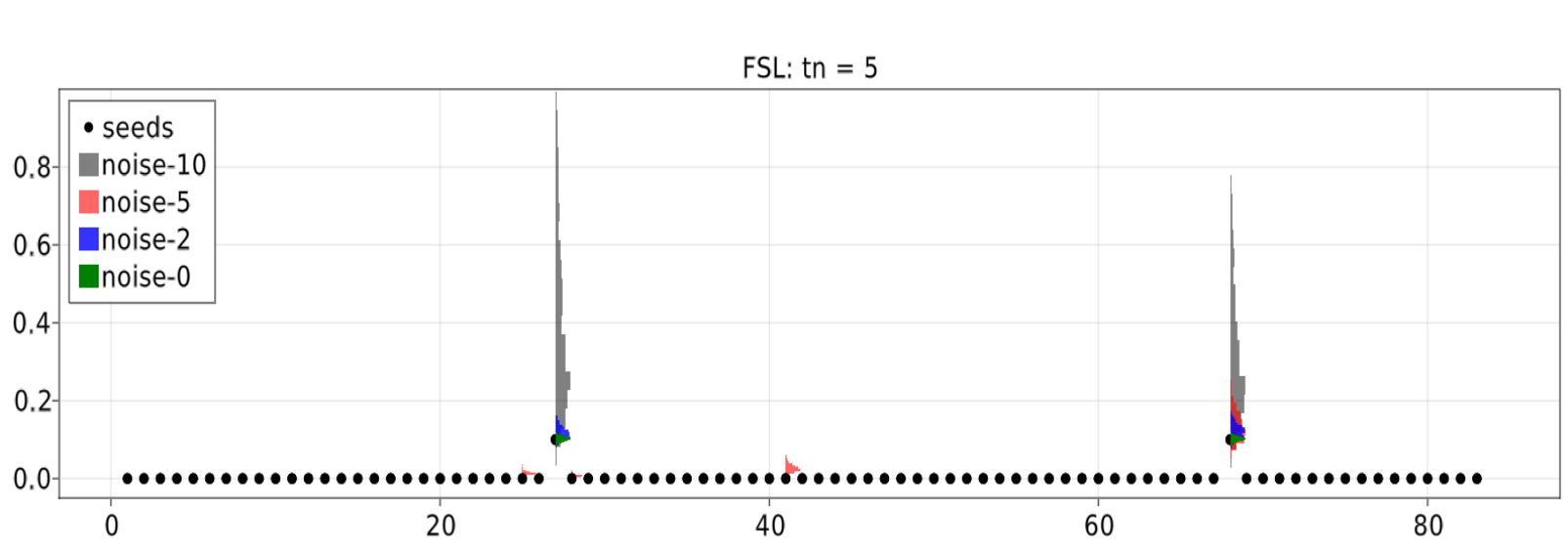
$t_{n=3}$

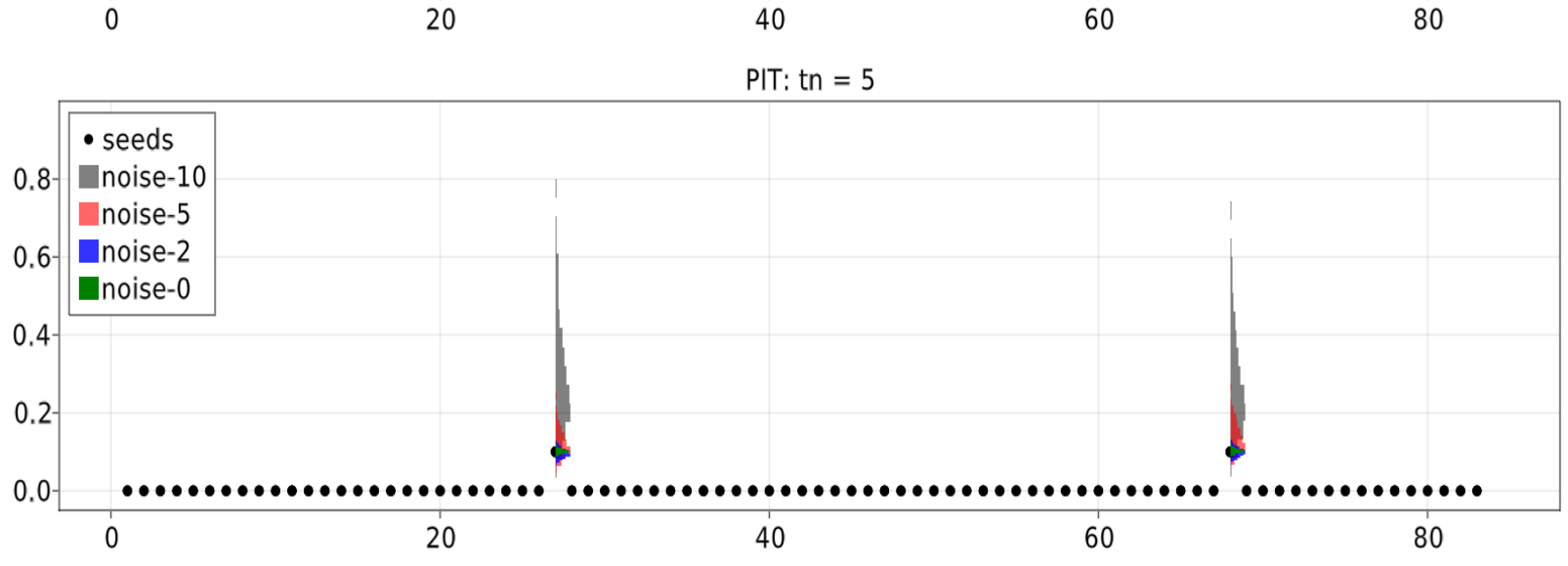




$t_{n=5}$

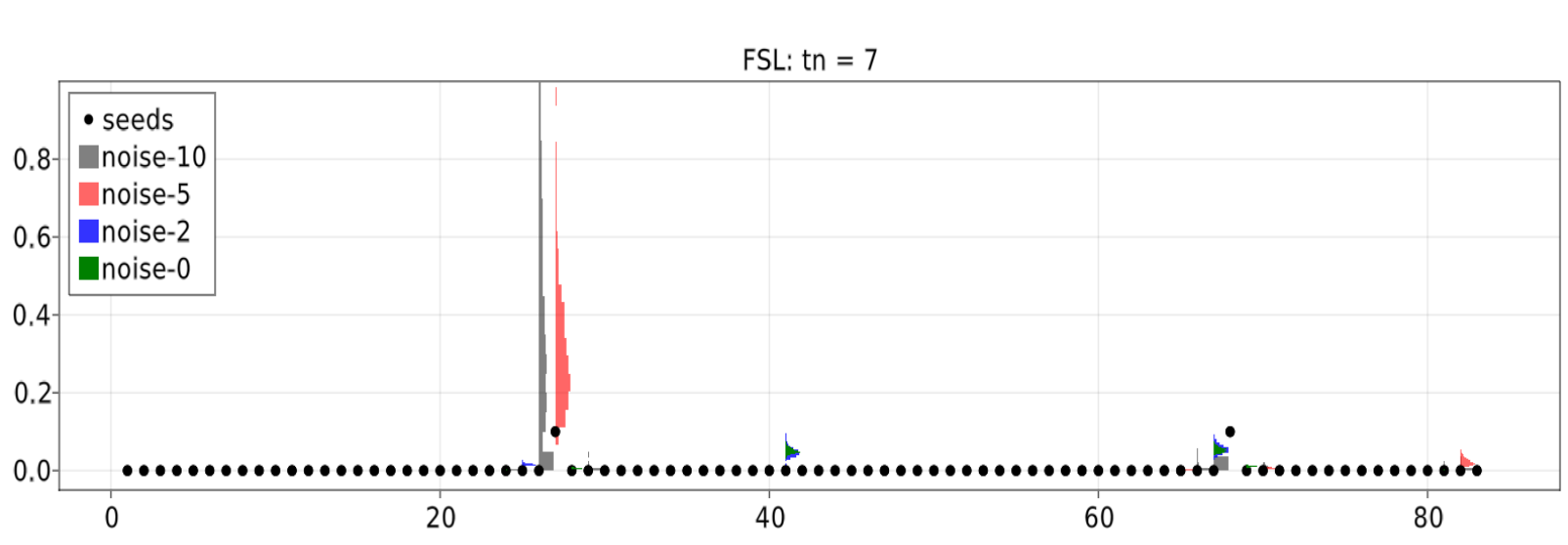
At $n = 5$, the locations of initial seeding are located in the PIT connectome but not the FSL connectome, again with high for high noise levels. In the FSL connectome, the left EC is identified in all noise cases; the right EC is identified in all but noise = 0.05.

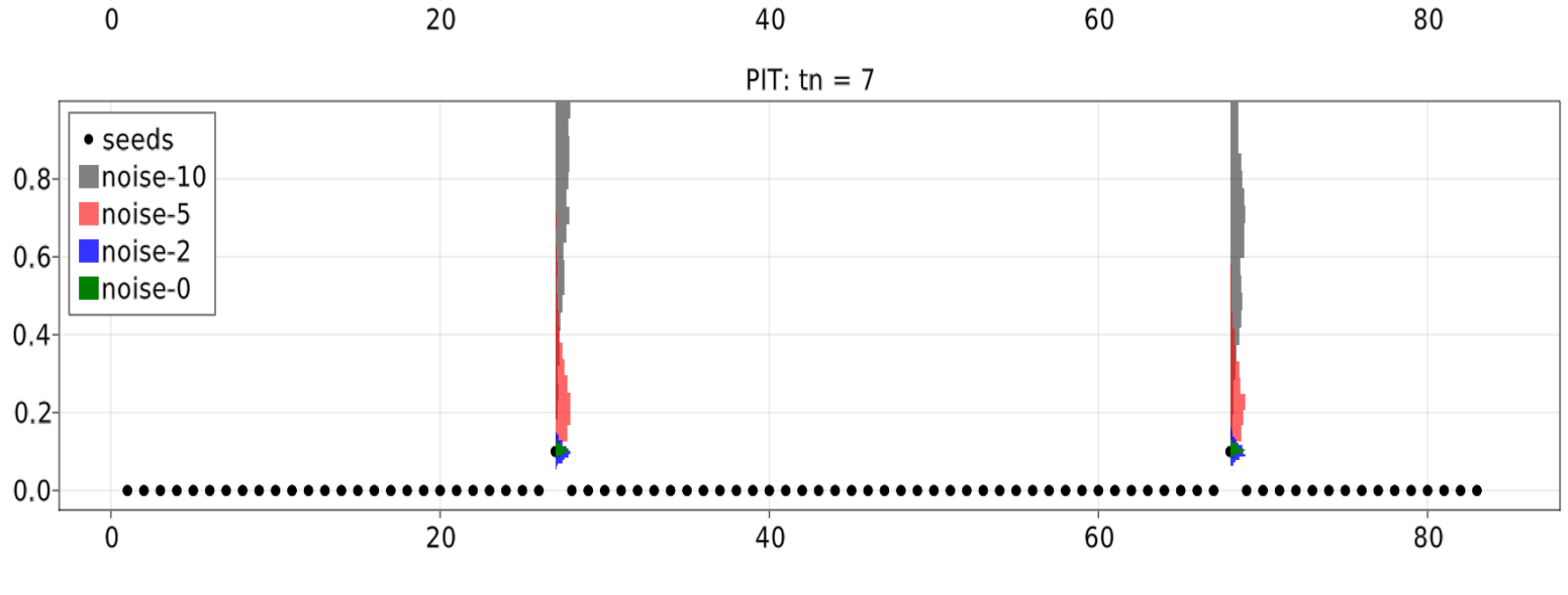




$t_{n=7}$

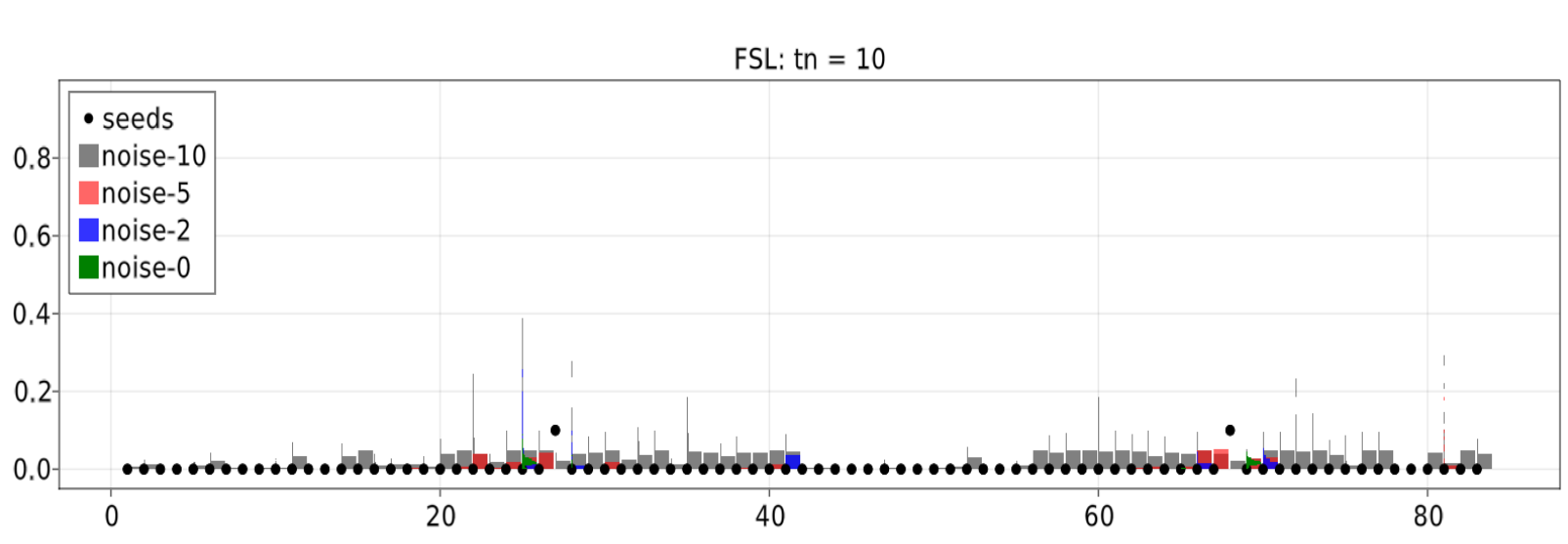
At $n = 7$, the initial conditions are poorly identified in the FSL connectome. At low noise levels, initial conditions are identified well in the PIT connectome, but at higher noise levels there is substantial uncertainty.

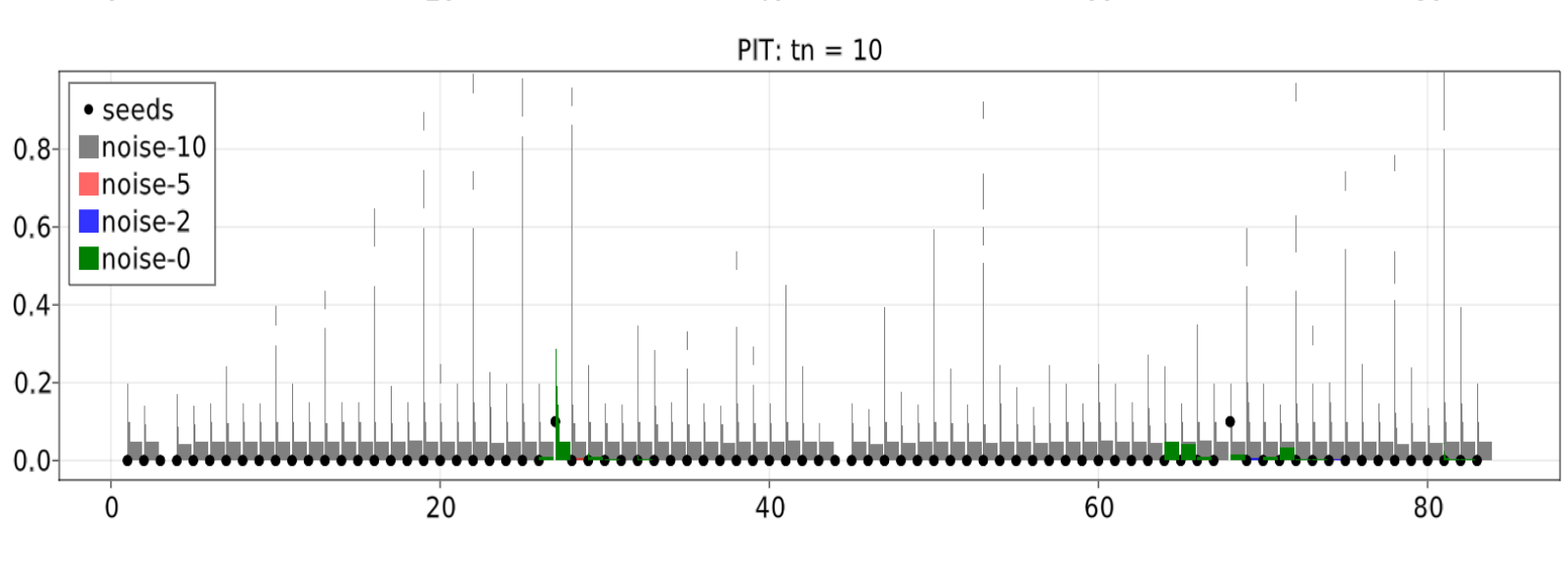




$t_{n=10}$

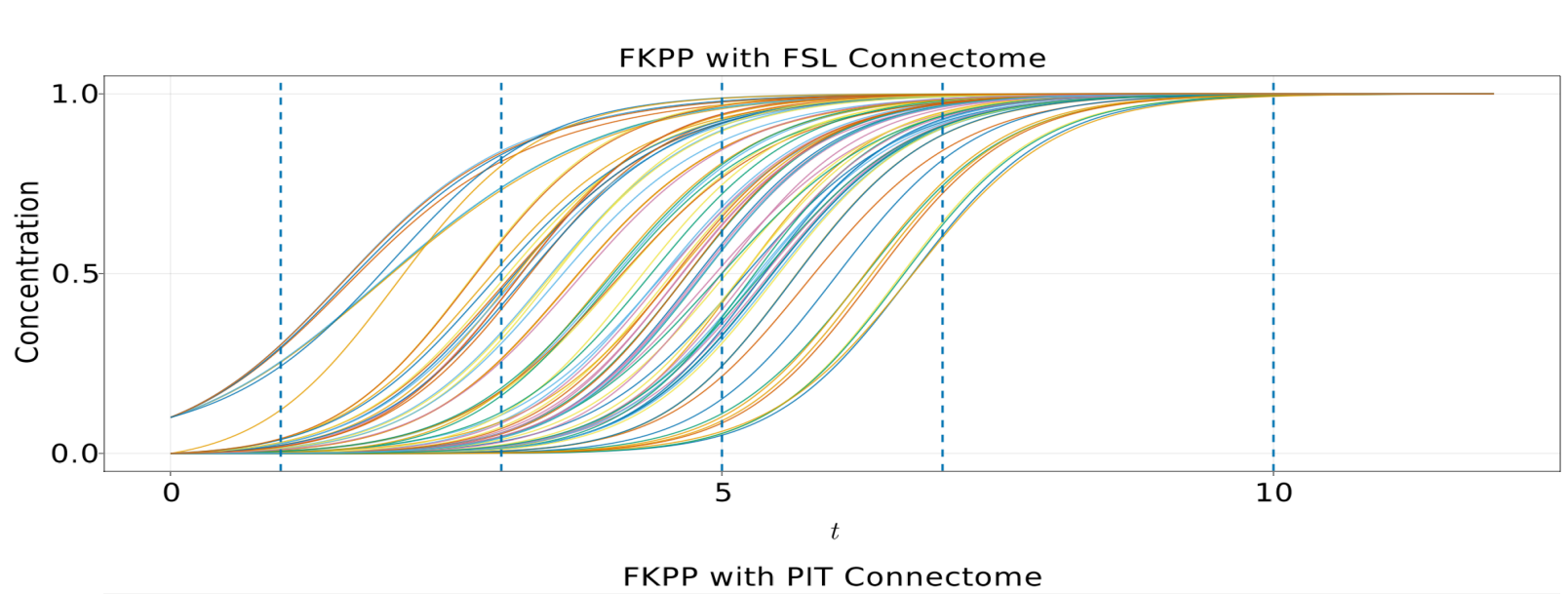
At $n = 10$, initial conditions are not identifiable in either the FSL or PIT connectome.

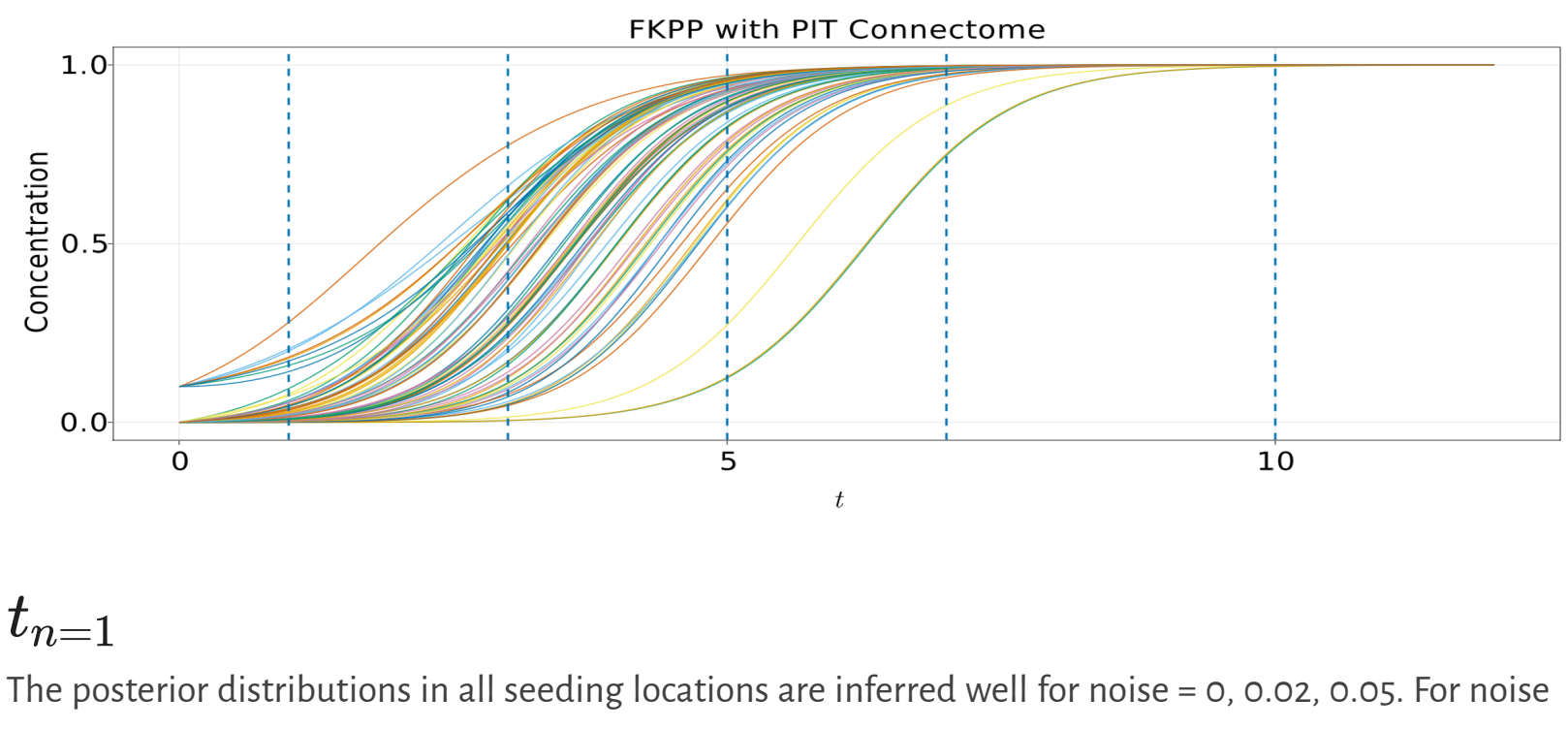




Random Seeding

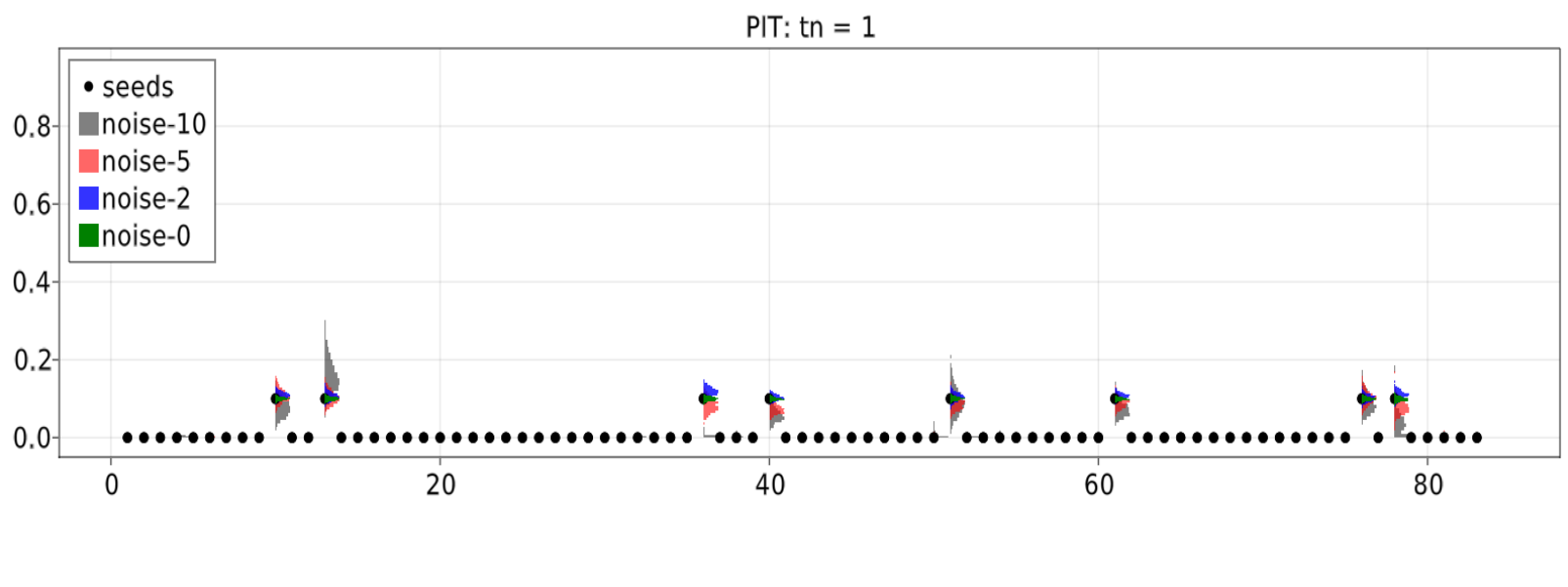
In the following experiments, I test the identifiability of 8 random initial seeds given different time intervals t_n. As before, data is generated with an FKPP simulation with $\rho = 0.5$ and $\alpha = 1.5$. Initial seedings sites are selected randomly and are the same for all tests. Given the poor identifiability of the EC at $n = 7$ and $n = 10$, results for these are not shown for this test case. Similarly to simulating with seeding in the EC, the trajectories on the FSL connectome are slower and more progressive.

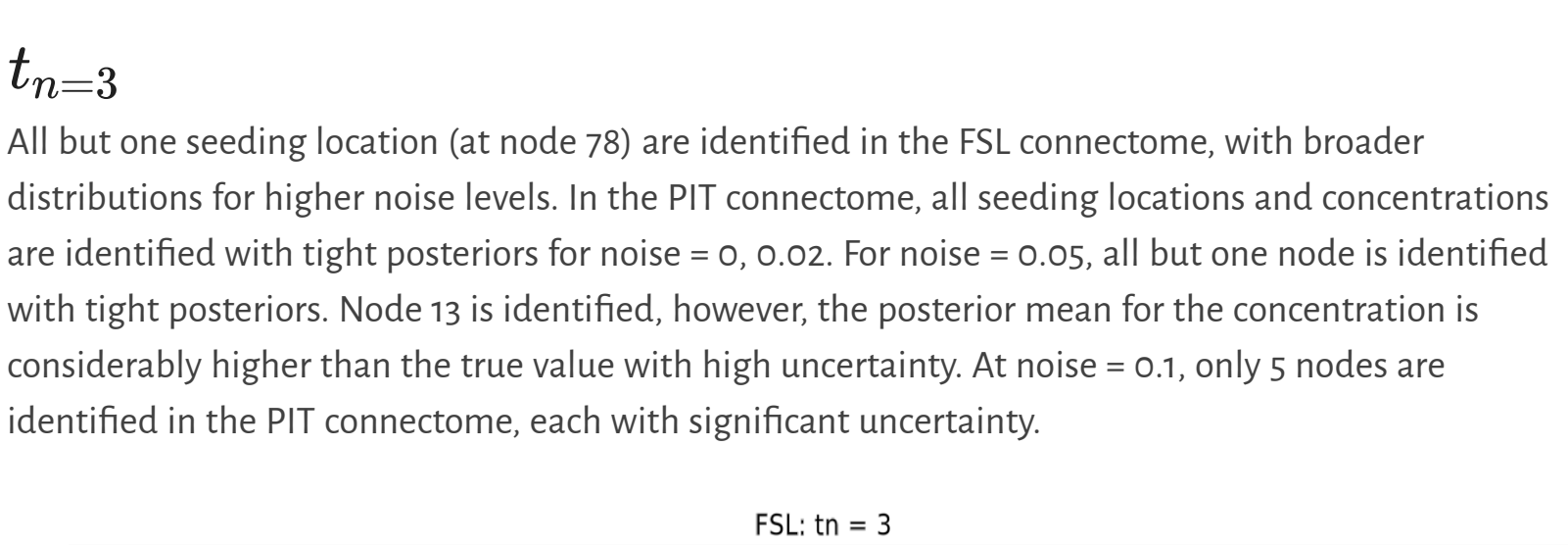




$t_{n=1}$

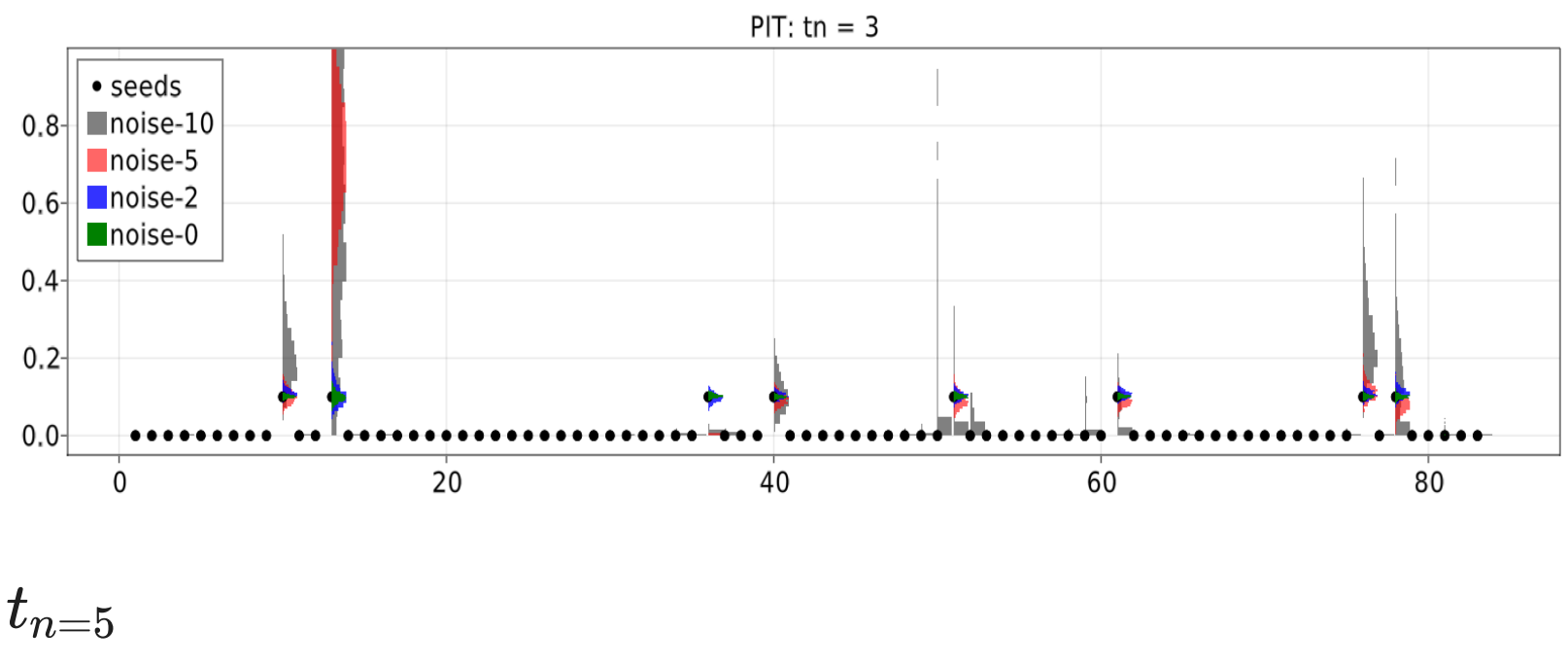
The posterior distributions in all seeding locations are inferred well for noise = 0, 0.02, 0.05. For noise = 0.1, posteriors are broader, but the initial seeding locations are identified.

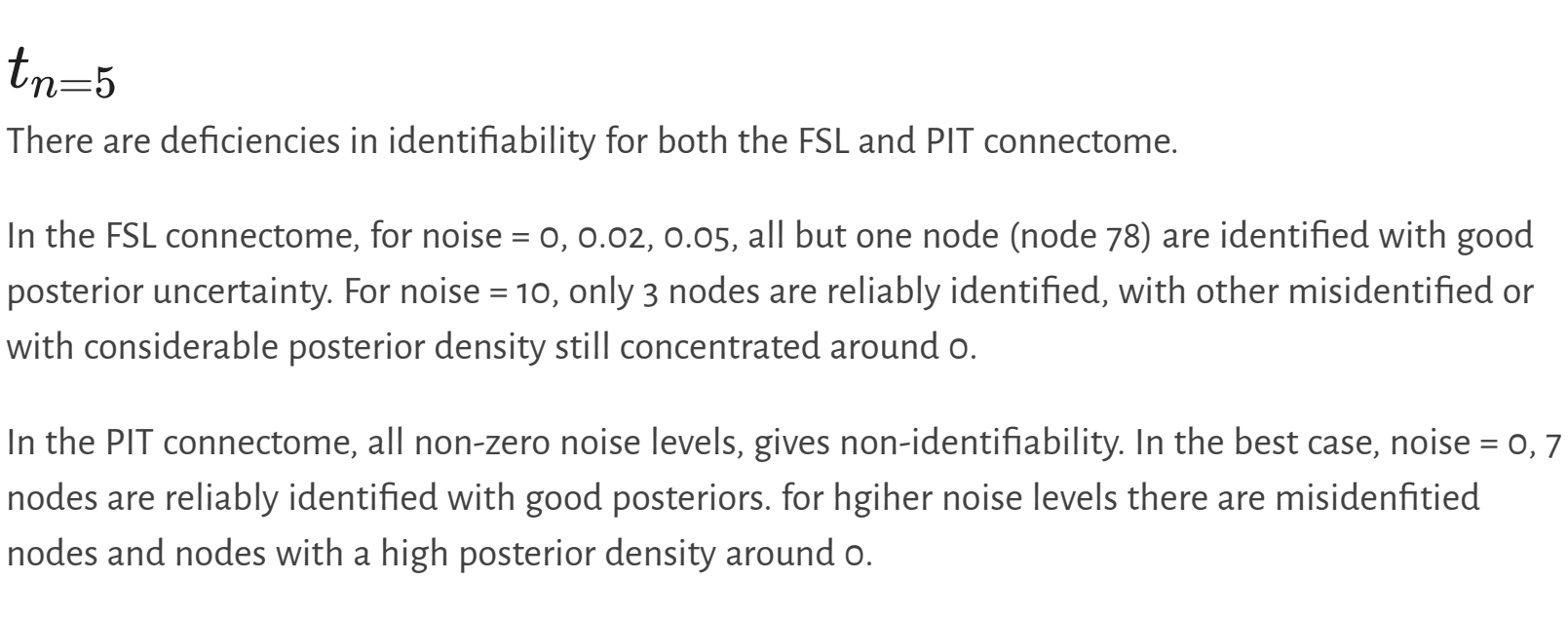




$t_{n=3}$

All but one seeding location (at node 78) are identified in the FSL connectome, with broader distributions for higher noise levels. In the PIT connectome, all seeding locations and concentrations are identified with tight posteriors for noise = 0, 0.02. For noise = 0.05, all but one node is identified with tight posteriors. Node 13 is identified, however, the posterior mean for the concentration is considerably higher than the true value with high uncertainty. At noise = 0.1, only 5 nodes are identified in the PIT connectome, each with significant uncertainty.





$t_{n=5}$

There are deficiencies in identifiability for both the FSL and PIT connectome.

In the FSL connectome, for noise = 0, 0.02, 0.05, all but one node (node 78) are identified with good posterior uncertainty. For noise = 10, only 3 nodes are reliably identified, with other misidentified or with considerable posterior density still concentrated around 0.

In the PIT connectome, all non-zero noise levels, gives non-identifiability. In the best case, noise = 0, 7 nodes are reliably identified with good posteriors. for hgiher noise levels there are misidenfitied nodes and nodes with a high posterior density around 0.