# Computational Roles of Intrinsic Synaptic Dynamics

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## Abstract

Conventional theories assume that long-term information storage in the brain is implemented by modifying synaptic efficacy. Recent experimental findings challenge this view by demonstrating that dendritic spine sizes, or their corresponding synaptic weights, are highly volatile even in the absence of neural activity. Here we review previous computational works on the roles of these intrinsic synaptic dynamics. We first present the possibility for neuronal networks to sustain stable performance in their presence and we then hypothesize that intrinsic dynamics could be more than mere noise to withstand, but they may actually improve information processing in the brain.

## Highlights

- Synapses exhibit changes due to intrinsic as well as extrinsic dynamics

- Computational frameworks suggest stable network performance despite intrinsic changes

- Intrinsic dynamics might be beneficial to information processing

## Introduction

Learning is a major area of research in both neuroscience and machine learning. Synaptic plasticity, changes in synaptic weight depending on the activity of neurons, is an essential mechanism for learning and memory in the brain [1]. One of the prevailing properties of synaptic plasticity is characterized by Hebb's rule [2,3], in which synaptic weights change according to the correlation between pre- and postsynaptic neuronal activities. Hebbian plasticity, including long-term potentiation and depression [1] and variants such as spike-timing-dependent plasticity (STDP) [4,5], has been proposed to contribute to efficient information processing in the brain. Further, being originally inspired by operations of neurons in the brain, artificial neural networks (ANNs) have been investigated as a promising subject in machine learning. Synaptic weights are trained in ANNs by an algorithm to achieve optimal performance (e.g., by the error back-propagation rule [6]). Although there are differences in the learning rules used in the brain and ANNs [7], the importance of changing the synaptic weight is established.

The postsynaptic counterpart of the synapse that receives a signal from the presynaptic neuron is called the dendritic spine, a small protrusion from a neuron's dendritic shaft (Figure 1A) [8]. Previous experimental results showed that the spine volume of a synapse is closely correlated with its weight [9–12], and synaptic plasticity protocols such as long-term potentiation and depression [13–16] and STDP [17,18] induce spine enlargement or shrinkage. Several in vivo studies have demonstrated that behavioral learning involves change in spine volumes and numbers [19–21] and that the selective shrinkage of the spines potentiated during training causes memory erasure [22]. These experiments give strong evidence that spines play a fundamental role in both learning and memory via Hebbian plasticity.

However, many studies have reported that spines are highly volatile (Figure 1B) [23,24]. About 40% of the spines in the hippocampus are replaced within 4 days [25] and more than 50% of

the spines in the auditory cortex are replaced within two weeks [26]. The volume of existing spines also exhibits substantial variability [27]. Although this variability can partly be explained by the effect of neuronal activities, spine volumes change significantly in an activity-independent manner as well. Several studies reported that spine sizes [28] or postsynaptic density molecules [29] fluctuate even under the condition where neuronal activities were inhibited pharmacologically. Spine formation and elimination under the suppression of neuronal activities were also observed in *in vivo* studies [30]. Surprisingly, one study reported that more than half of the changes of individual spines are estimated to occur independently of the neuronal activities by analyzing the size correlation of spines between the same pre- and postsynaptic neurons [31]. Note that, in contrast to the intrinsic dynamics, we call synaptic changes due to activity-dependent synaptic plasticity extrinsic synaptic dynamics hereafter.

The existence of intrinsic synaptic dynamics raises two important questions. First, how is memory retained in the presence of intrinsic dynamics? While many studies have attributed memory to synaptic weight, some recent works have suggested stability of memory under spine fluctuations. Second, do intrinsic dynamics provide benefits for information processing in the brain? Generally, fluctuations can play an important role for biological processing such as reinforcement learning with stochastic synaptic transmission [32] and selecting a suitable gene expression attractor with noise [33]. Recent theoretical and experimental studies on intrinsic spine dynamics further suggest their benefits for statistical inference, stable memory, and exploration in reinforcement learning. We address these questions by reviewing several studies on intrinsic spine dynamics.

## Some synaptic fluctuations might be harmless.

Several theoretical frameworks have been proposed to explain the stability of brain function despite the volatility of its elements. Some frameworks simply suggest that brain function is

insensitive to the fluctuations of (at least a part of) synapses (Figure 2A). It has been experimentally

verified that the stability of dendritic spines varies across spine age, size, morphological features, or

expression of molecular markers [26,34]. Therefore, stable memory could be maintained via those

relatively stable synaptic connections. Different computational models requiring stability of only a

subset of synapses for memory maintenance support this idea [35–38]. For example, a computational

study using a cortical circuit model of spiking neurons [36] showed that rewiring of excitatory

connections had much less influence on the network activity compared with rewiring of inhibitory

connections under the condition that the firing rates of the inhibitory neurons are higher and more

diverse than those of the excitatory neurons in the balanced network. Another line of works focusing

on the prevalence of multisynaptic connection [39,40] suggests that while traces of neuronal activity

via Hebbian or other types of plasticity rules naturally correlate among synapses between the same

pair of neurons, intrinsic factors are independent with each other. Thus creating multiple synaptic

contacts could partly cancel the perturbation caused by intrinsic dynamics [41–43].

Similar but slightly different perspectives emphasize the importance of finding a suitable

structure of network connectivity rather than optimizing each synaptic weight parameters. If network

performance primarily depends on its configuration, synaptic fluctuations that do not alter its

structural pattern can be harmless. In the field of neuroscience, connectome studies aim to draw a

comprehensive "wiring diagram" of the brain [44]. It has been demonstrated that many features of

network architectures, both local and global, are highly preserved among individuals of the same

species [45], and abnormal connectivity is reported to be linked to various psychiatric disorders [46].

This robust reproducibility of connectome, which cannot be fully explained by random network

models [45], argues for the importance of the network structure. This view is also supported by

insights in the field of machine learning; empirical relationship between suitable network structures

and task domains are widely known (e.g., convolutional neural network (CNN) - image processing

[47], long short-term memory (LSTM) - time series [48]), and several works demonstrated that architectures with such strong inductive bias could perform well even when their weights are randomly assigned. For instance, a randomly-initialized CNN was capable of effective image processing [49,50], and randomly-initialized LSTM combined with a learned linear output layer was able to predict time series accurately [51]. A recent work by Gaier and Ha [52] generalized this idea to propose a generic algorithm to search for architectures that could perform well over a wide range of weights. Their algorithm is a variant of evolutionary computing for topology search, starting from simple initial status and evolving network architectures incrementally based on their average performance over a set of different weight parameters. Altogether, these works raise the possibility that fluctuations in synaptic weights can be mitigated under a certain condition, as long as the qualitative characteristic of network connectivity is preserved.

## Intrinsic dynamics could contribute to brain function.

In the previous section we reviewed work supporting the idea that (some) synaptic fluctuations may be harmless under certain conditions. An implicit assumption behind them is that spontaneous fluctuations are undesirable noises, which in principle lead to deterioration of the performance. Considering the significant magnitude of intrinsic dynamics [31,53], however, one could suspect an opposite case. Below we focus on this possibility, that is, intrinsic dynamics may be more beneficial than harmful. We review this possibility for representing probabilistic information, maintaining memory, or acquiring new information.

*Statistical inference via synaptic stochasticity.*

As we all know, life is full of uncertainty: the external world is innately irregular, and available information on the environment is always imperfect and noisy. For animals to survive, they

must handle this uncertainty. This observation leads to a widely accepted theory called the Bayesian brain hypothesis [54], which states that the brain can efficiently represent and manipulate stochasticity. Experimental results have verified that the brain can conduct probabilistic inference at near Bayesian-optimal level [55], and several models are proposed at the synaptic [56–58], neuronal [59–61], circuit [62–65], or cognitive [66–68] levels. Among these, the sampling hypothesis states that a "snapshot" of neural activity is a draw from the encoded distribution [69]. Here we highlight recent works that utilize synaptic fluctuations as the driving force for sampling a "snapshot" (Figure 2B).

In a series of works by Kappel et al. [70,71], they modeled synaptic dynamics as a variant of Langevin sampler [72], which asymptotically represents the posterior distribution. These dynamics allowed synaptic parameters, although changing continuously and stochastically, to remain mostly within a high-dimensional region of high posterior probability (in the setting of unsupervised learning [70]) or large expected reward (in the setting of reinforcement learning [71]), while maintaining computational performance in the presence of ongoing synaptic dynamics. The derived synaptic update algorigthm reproduced a (reward-modulated) STDP plasticity rule [73,74] as well as showing good generalization ability and robustness to perturbation due to its Langevin dynamics.

Another interesting perspective was introduced by integrating stochasticity at the synaptic and neuronal levels to draw samples from the encoded distribution [75]. Here, it was shown that the fluctuations of both neural activity and synaptic weights work as the Gibbs sampling [76], generalizing learning in Boltzmann machines [77] with additional weight sampling. The derived algorithm reproduced several non-trivial experimental findings, such as the power-law coding of the cortex [78], at the neural activity level and was consistent with STDP rule at the synaptic level.

*Homeostatic effect of intrinsic dynamics.*

Previous findings, both experimental and theoretical, suggest intrinsic dynamics may have another benefit: homeostasis of synaptic weight distribution (Figure 2C). Many experimental works have consistently reported that the distribution of synaptic weights (or the corresponding dendritic spine volumes) have a unimodal, heavy-tailed, and skewed shape (for review, see [79–81]; note that the tail of the distribution is cut off at the upper bounds of spine size ($\sim 1 \mu m^3$)). This stereotypical shape seems almost universally preserved, even in the extreme conditions where neuronal networks developed in the absence of synaptic transmission [82,83], spiking activity [28,53], or expression of key molecules for physiological neuronal development [84–86]. While the functional significance of this distributional feature is not yet completely understood, several computational works have highlighted its contribution to efficient information transmission [87,88], enriched repertoires of activity patterns [89], and criticality in the brain [90].

The classical model of Hebbian plasticity, however, struggled to maintain the distribution of synaptic weights due to its positive feedback effects [91,92], and previously proposed variations of plasticity rule without intrinsic dynamics [93–95] cannot fully explain the robustness of the distribution. In contrast, simple modeling of the intrinsic dynamics as a diffusion process, which well captures experimental observations, suffices to reproduce the characteristic weight distribution robustly in both physiological [27,28,53] and pathological conditions [84] (Figure 2C). The analysis of this diffusion process yields that skewness and heavy-tail should be attributed to the fact that the magnitude of intrinsic dynamics is approximately proportional to synaptic weight [28].

Furthermore, a recent study [96] suggests that intrinsic dynamics, when interacting with extrinsic ones, could maintain memory by introducing bistability in a group of synaptic weights. In a recurrent network model of spiking neurons, their appropriate combination allowed formation and maintenance of cell assemblies (i.e., groups of strongly connected and coactive neurons) that encoded memory. The combination created a separation point between large and small synapses to

minimize their interconversion, separating strong intra-assembly and weak non-intra-assembly synapses while roughly confining the synaptic weight distribution to a stereotypical shape (Figure 3A). Although the influence of having cell assemblies to the weight distribution looks small in the standard linear plot, it is magnified and form a secondary peak in the semi-logarithmic plot (Figure 3B). Importantly, such a secondary peak was experimentally detected only recently by the advancement of serial section electron microscopy (ssEM) [43,97]. These findings hint that the brain might effectively use two 'representative' spine sizes, echoing older suggestions on binary synaptic states [98], and the utility of binary synapses in high-performance ANNs [99]. An additional important property of the above model is that individual synapses do not take independent binary states—rather, most intra-assembly synapses take the strong state, and most non-intra-assembly synapses take the weak state.

## *Exploration via Intrinsic dynamics?*

Another underexplored potential of intrinsic synaptic dynamics is to enhance exploration. Since the exploration-exploitation trade-off is a key concept in reinforcement learning, engineeringly many algorithms have been proposed to ensure exploration of the agent. Among them, adding random (and reward- or environment-independent) noise to the policy parameters is simple to implement and has exhibited impressive performance in various settings [100,101]. The advantage of perturbations for enhanced exploration has also been studied in neuronal models, but these studies sought the origin of perturbation for the exterior of the learning network [102], stochasticity of presynaptic vesicle release [32], or intrinsic excitability of neurons [103,104]. While direct evidence remains elusive, synaptic fluctuations might be a novel mechanism to implement exploratory behavior in neuronal networks.

*A link to another dynamics in the brain: representational drift.*

So far we have mainly discussed brain dynamics at the synaptic level. However, other dynamic features of information processing in the brain are drawing attention as well. In particular, several experimental works have demonstrated that neuronal representation, which refers to the neural activity specifically related to each memory, is continuously drifting over time (for reviews of the relevant literature, see [105,106]). The drift seems ubiquitous across many brain areas including hippocampus, sensory cortex and motor cortex, even when the animal shows no apparent change in its behavior. The cause and role of representational drift largely remain unknown. Some modeling works have proposed the framework in which extrinsic synaptic dynamics change neural codes to be consistent with the learning criterion and intrinsic dynamics add isotropic random changes, thereby the representation drifts in the "neutral" dimensions of the learning criterion [71,107]. For example, the network model of [71] was driven by both intrinsic dynamics and the gradient of expected reward. As a result, while the action and rewards were almost identical over trials after learning completion, the neural representation encoding such action was continuously drifting. Experimental evidence to support this idea is not sufficient at present, but the combination of intrinsic and extrinsic synaptic dynamic might be crucial for the brain to be both adaptive and flexible.

## Conclusion

In this work we reviewed recent developments, based on both experimental and modeling tasks, on the computational roles of intrinsic synaptic dynamics. While conventional rules of neural plasticity attempt to describe synaptic weight changes based on neural activities, here we propose that the widespread presence of activity-independent synaptic fluctuations warrants the investigation of intrinsic dynamics to characterize the changes. In some previous works it is assumed (although often only implicitly) that intrinsic dynamics do not compromise network performance. Different

insights from neuroscience and machine learning, however, raise the possibility that brain dynamics

not only are constantly affected by intrinsic dynamics but could benefit from their presence. Future

theoretical and experimental studies might give us the understanding of why our brain evolutionarily

has chosen to develop neural networks based on intrinsically dynamical components.

Figure legend

Figure 1

A schematic image of dendritic spines and spine fluctuations.

A. Presynaptic neurons transmit information to postsynaptic neurons through synapses. The postsynaptic sites of excitatory synapses mostly form dendritic spines, small protrusions on dendritic shafts. Synaptic weights are nearly in proportion to spine volumes, and potentiation/depression of synapses are associated with enlargement/shrinkage of dendritic spines.

B. The spine size is regulated by two factors: extrinsic dynamics (activity-dependent plasticity) that reflects neuronal activities and intrinsic dynamics (fluctuation) that is independent of neuronal activities. Note that for larger spines intrinsic dynamics is dominant, while smaller spines are rather subject to extrinsic dynamics.

Figure 2

Examples of various computational perspectives on intrinsic dynamics.

A. Information might be mainly stored in the subset of neurons and synapses, and modifying the rest could be harmless. In the schema, memory is stored in the neurons and synapses in the right population (blue). As a result, rewiring synaptic connections in the right population impairs memory, while rewiring in the left (orange) does not. For example, in the case of computational modeling work by [36], rewiring excitatory synapses did not hinder memory recall whereas rewiring inhibitory synapses did. Note that they used balanced cortical network model with the average firing rate higher and more diverse in inhibitory neurons, and also they assumed that cell assemblies were formed via anti-Hebbian plasticity of inhibitory synapses as well as Hebbian plasiticy of excitatory neurons.

B. It is widely accepted that the brain represents and manipulates uncertainty in various ways. The framework proposed by Kappel et al. [70,71] suggests that combination of extrinsic and intrinsic dynamics could work as sampling dynamics from the target distribution of possible network connectivity.

C. The skewed and heavy-tailed distribution of synaptic weights naturally arises from modeling synaptic dynamics as a stochastic process. If we use Brownian motion to describe the randomness of synaptic dynamics, fluctuations with an average change $\mu(w)$ and a standard deviation $\sigma(w)$ can be described by a stochastic differential equation $dw = \mu(w)dt + \sigma(w)dB_t$ (where $B_t$ represents standard Brownian motion). The drifting term $\mu(w)$ and diffusion term $\sigma(w)$ were measured in various conditions, with which the stationary distributions of synaptic weights could be obtained. (orange): control condition [28,84]. (blue): silenced condition [28]. (green): Fmr1 knockout (KO) condition, which is a mouse model for autism spectrum disorder (ASD) [84]. The distribution have common skewed and heavy-tailed shape in all conditions. The smaller spines observed in Fmr1 KO model is explained by the enhanced spine turnover (larger $\sigma(w)$). Note that the plots are schematic illustrations that approximate but do not exactly replicate original fittings.

Figure 3

Normal and semi-logarithmic plots of spine sizes and their multi-stability. The data is from Figure 3E of the ref [96], in which synaptic weight $w$ is proportional to spine size.

A. A standard plot of synaptic weight distribution $f(w)$. Even after stable memory formation was achieved by the cell assemblies, the model yielded the monotonously decaying stationary distributions for synaptic weights.

B. A semi-logarithmic plot of synaptic weight distribution. Following the coordinate transformation,

the distribution is given by $\left|\frac{\mathrm{d}\log w}{\mathrm{d}w}\right|^{-1} f(w) = w f(w)$. It displayed an additional peak at large synaptic weight if cell assemblies are embedded. This was because the semi-logarithmic plot magnified the nearly invisible difference in (A) for the distributions with and without cell assemblies. Note that the major peak around $\log w = -3.0$, which is absent in $f(w)$, was produced by the coordinate transformation.

## Conflict of interest statement

The authors declare no conflicts of interest.

## References and recommended reading

Papers or particular interest, published within the period of review, have been highlighted as:

\*          of special interest

\*\*         of outstanding interest

## Acknowledgements

*(annotations for selected literatures)*

[28] (Yasumatsu et al., J Neurosci 2008)

(\*) The first report of intrinsic synaptic dynamics. The authors observed, using chronic two-photon

imaging, that dendritic spine volumes fluctuated even after the total pharmacological blockade of neural activities in hippocampal slice cultures, and the fluctuations quantitatively account for the statistics of spine volumes using stochastic differential equations.

[30] (Nagaoka et al., Sci Rep 2016)

(*) First study to report that intrinsic dynamics is also present in vivo, using chronic two-photon imaging with cortical activity silenced only locally. They also reported that enhanced synaptic turnover rate in Fmr1 KO model mice primarily reflected elevated level of intrinsic dynamics.

[36] (Mongillo et al., Nat Neurosci 2018)

(**) The authors showed in the balanced network model of cortical circuit that rearranging inhibitory connectivity more significantly altered network activity patterns than excitatory connections in the condition that time-averaged firing rate is higher and more diverse in inhibitory neurons. Note that in applying this argument to memory maintenance and recall they assumed anti-Hebbian plasticy in inhibitory synapses.

[43] (Dorkenwald et al., bioRxiv 2019)

(*) The large connectivity map between layer 2/3 pyramidal cells in mouse primary visual cortex was presented using ssEM technique. They showed synapse sizes could be modeled by the sum of a binary variable and an analog variable drawn from a log-normal distribution and suggested that the former result from activity-dependent plasticity rule while the latter reflect intrinsic dynamics.

[60] (Echeveste et al., Nat Neurosci 2020)

(*) In the article, the authors trained a canonical balanced neuronal network model of sensory cortex for a sampling-based inference, and found the optimized network exhibited various cortical-like dynamical features, such as gamma-oscillations, stimulus-modulated noise variability, transient overshoots at stimulus onset.

[61] (Aitchison et al, Nat Neurosci 2021)

(*) The authors propose a novel synaptic plasticity rule in which both synaptic weights and their uncertainty are updated via learning. The proposed normative rule shows larger learning rate when the uncertainty about synaptic weight is larger; in other words, the less confidence a synapse has in its target weight, the larger influence new information has on its update. They further suggest that this uncertainty is represented as the variability in the postsynaptic potential size.

[71] (Kappel et al., eNeuro 2018)

(**) The authors proposed a framework to regard synaptic fluctuations as a sampling dynamics. Via combination of reward-modulated plasticity and intrinsic dynamics, the network could move mostly within the configuration region of high expected reward under ongoing synaptic changes.

[75] (Teramae. bioRxiv 2020)

(**) The author hypothesized that the brain were generating synaptic and neural states that were consistent with external world. More precisely, they formulated that both firing of neurons and formation of synapses were the result of Gibbs sampling conditioned on the external environment and the status of other neurons and synapses. This perspective could be regarded as the extension of Boltzmann machine learning with additional synaptic sampling. This framework predicted the existence of retrograde modulation by postsynaptic neurons, as well as consistently explained various experimental findings in the brain.

[84] (Ishii et al., eNeuro 2018)

(*) The authors recorded spine dynamics of Fmr1 KO mice, which are one of the animal models of ASD, in visual cortex using in vivo chronic two-photon imaging. They reported that Fmr1 KO mice showed higher rate of spine fluctuations for the first time in vivo, which led to the predominance of smaller spines in Fmr1 KO mice.

[90] (Kusmierz et al., Phys Rev Lett 2020)

(*) A novel proposal for the computational role of heavy-tailed synaptic distribution. The authors

studied a random network model in which synaptic weights are drawn independently from the identical Cauchy distribution. The network showed continuous phase transition from a quiescent state to a chaotic state. Neuronal avalanches (i.e., bursts of activity with power-law distributions of sizes and lifetimes) were reproduced at the critical point (i.e. the edge of chaos). By contrast, the Gaussian counterpart showed a discontinuous jump to chaos under the assumption that neurons have firing threshold and receive many synaptic inputs, thus could not be posed robustly at the edge of chaos.

[96] (Humble et al. Front Comput Neurosci 2019)

(**) They showed combinations of Hebbian plasticity and intrinsic dynamics stabilized cell assembly while maintaining physiological heavy-tailed distribution of synaptic weight. This stable maintenance of cell assembly was impaired by strong intrinsic dynamics observed in some ASD models.

[100] (Fortunato et al., ArXiv 2019)

(**) The authors introduced NoisyNet, a deep reinforcement learning agent with probabilistic noises added on its weights aiming efficient exploration. Although straightforward to implement, this agent showed substantially better performance on a wide range of Atari games than conventional heuristic methods for exploration.

[107](Kalle-Kossio et al., bioRxiv 2020)

(**) In this modeling work, the authors suggested that representational drift was driven by spontaneous synaptic remodeling which caused transition of neurons between cell assemblies, while consistency of inputs – assembly – outputs relationship was maintained via Hebbian plasticity without requiring any additional teaching signals or behavioral feedback. They also reported that probabilistic firing of neurons contributed to drift as well, suggesting the importance of integrating the stochasticity of different levels.

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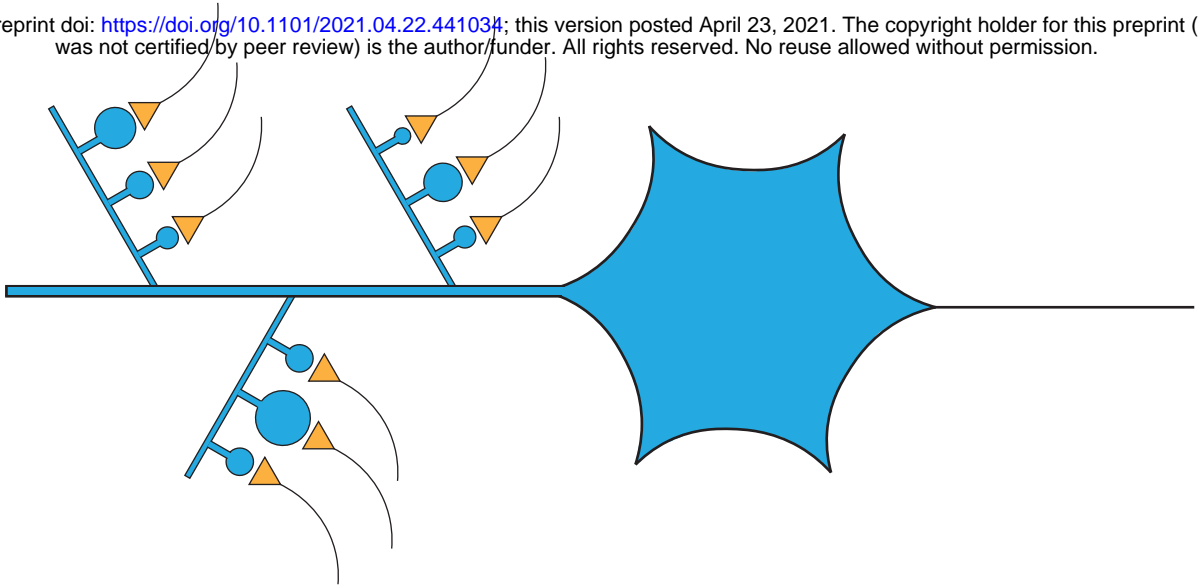
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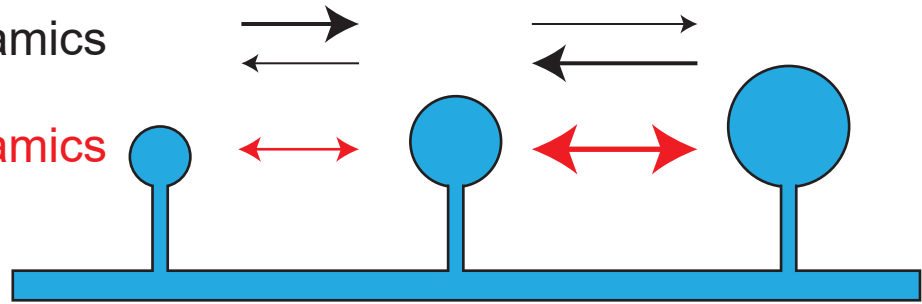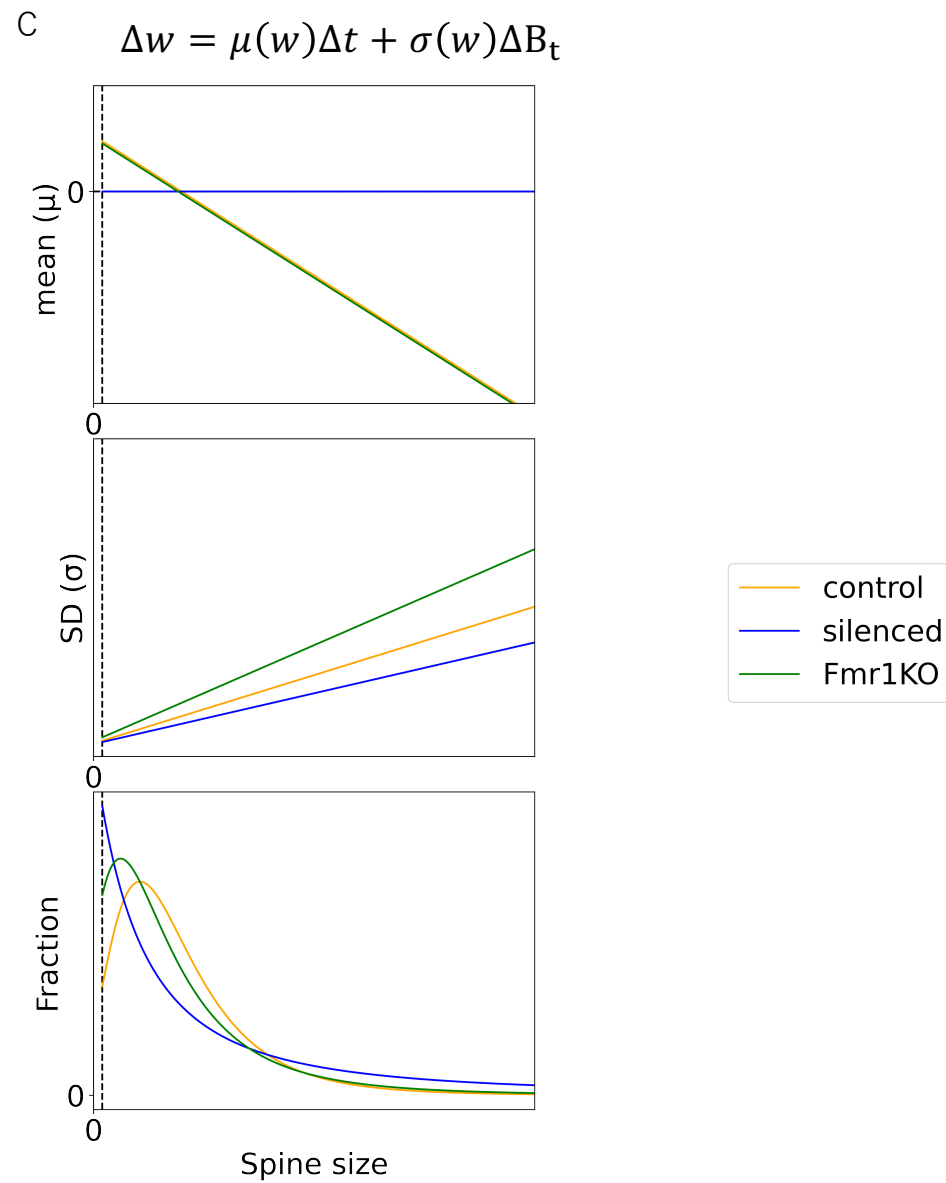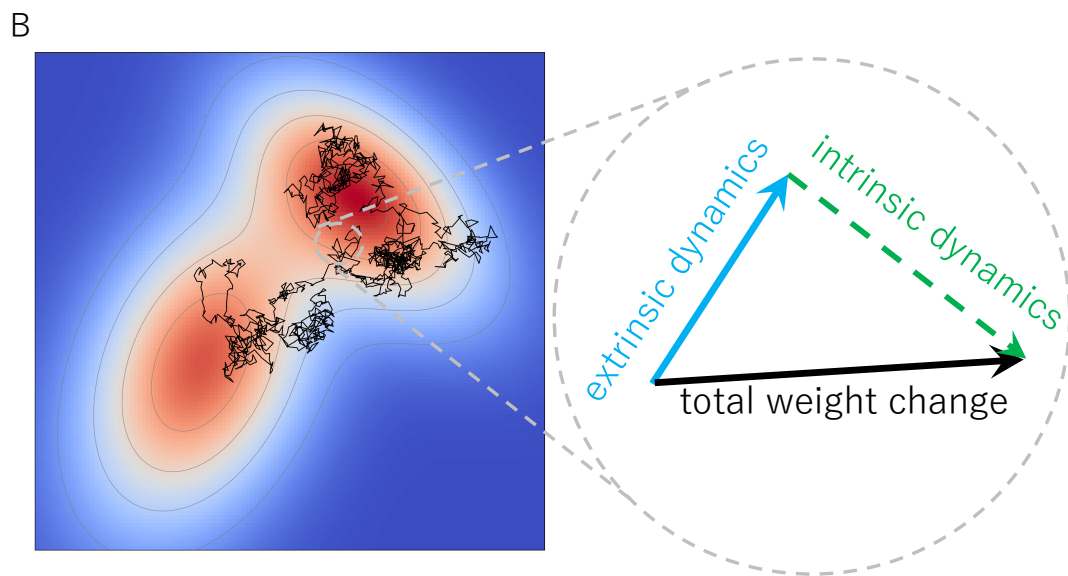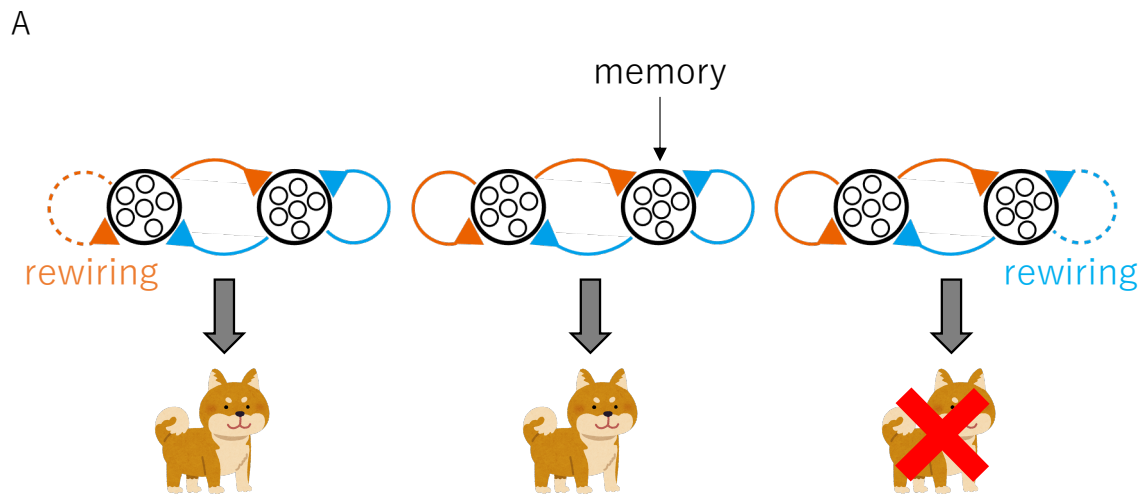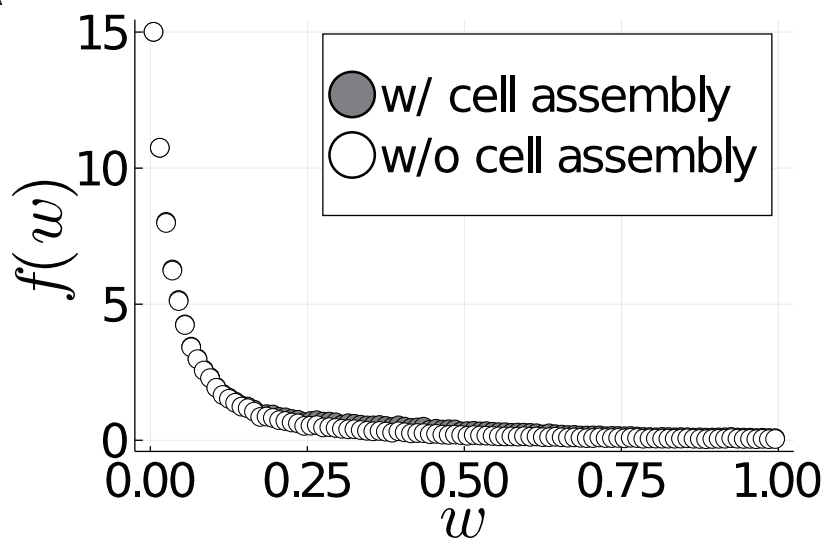
A

memory

rewiring                                         rewiring

B

extrinsic dynamics    intrinsic dynamics

total weight change

C

$$\Delta w = \mu(w)\Delta t + \sigma(w)\Delta B_t$$

mean ($\mu$)

0

SD ($\sigma$)

0

Fraction

0

0                   Spine size

control
silenced
Fmr1KO

A



B