# The Behaviour of a Hopfield Network Challenged with Spontaneous Noise

Schizophrenia is a complex condition, affected by a multiplex of neuronal abnormalities that can lead to the manifestation of hallucinations. This paper explores these mechanisms and provides the rationale to reduce the underlying biological drivers to a single metric, a reduced signal to noise ratio (SNR). The Hopfield network, a point attractor network, is modified here to investigate the behaviour of the resting state challenged with varying degrees of noise. If analogous attractor networks are present within the nervous system, a reduction in the SNR, which effectively reduces the barriers to traversing an energy landscape, may serve to explain how hyper excitability and spontaneous activation of internally stored states contribute to the manifestation of hallucinations in individuals affected by schizophrenia.

Nicholas Mikolajewicz
Ph.D. Student
Craniofacial Health Sciences
Shriners Hospital for Children
Faculty of Dentistry
McGill University

NEUR 603; Computational Neuroscience
Dr. Chris Pack

## 1| Introduction

Hallucinations are widespread. The list of underlying causes are endless, and so for the purpose of this paper, schizophrenia will be considered. With the latest edition of the DSM-V, classification of schizophrenia have been restructured so that hallucination no longer falls under the umbrella of positive symptoms, and is considered its own category in itself. However, even with this, hallucinations are a heterogeneous beast that can encompass many different flavours of perceptual distortion.

To construct a computational model that can emulate hallucinations, it is essential to understand what drives their manifestations, especially in the context of schizophrenia. Taking a brief historical detour back to the founding fathers of schizophrenia, Emil Kraepelin was first to describe this condition as Dementia Praecox ("Premature", 1896). He realized that that the condition manifests early and progressively deteriorates the mind over the course of one's life. It was, however, Eugen Bleuler (1911) who coined schizophrenia, arising from "schizo" (split) and "phrenia "(brain), to emphasize the disconnection from reality individuals experienced. Many years later, it is now widely accepted that schizophrenia is indeed a neurodevelopment disorder, contributed to by genetic and early-life environmental factors (Davis et al., 2016; Negron-Oyarzo, Lara-Vasquez, Palacios-Garcia, Fuentealba, & Aboitiz, 2016).

## 2| Biological Basis

The biological basis for schizophrenia can be separated into two branches of investigation, neuroanatomical and neurochemical. Having a look at the cortex, the grey matter density in adolescence youth, shortly after their first psychotic episode, has revealed a

consistent reduction in grey matter density (Figure 1a, Keshavan, Giedd, Lau, Lewis, & Paus, 2014). Moreover, twin studies, in which one twin is affected with schizophrenia, have identified abnormal enlargement of the ventricular cavities in affected individuals (Figure 1b, Ordonez, Luscher, & Gogtay, 2015). On a cellular scale, dendritic spine densities have been observed to be alarmingly reduced (Figure 1c, Garey, 2010). Taken together, the blunt reduction in the volume and density of the neuroanatomy observed in individuals affected with schizophrenia can be interpreted as a pathological disruption in synaptic architectures, and ultimately suggest weaker connectivity.

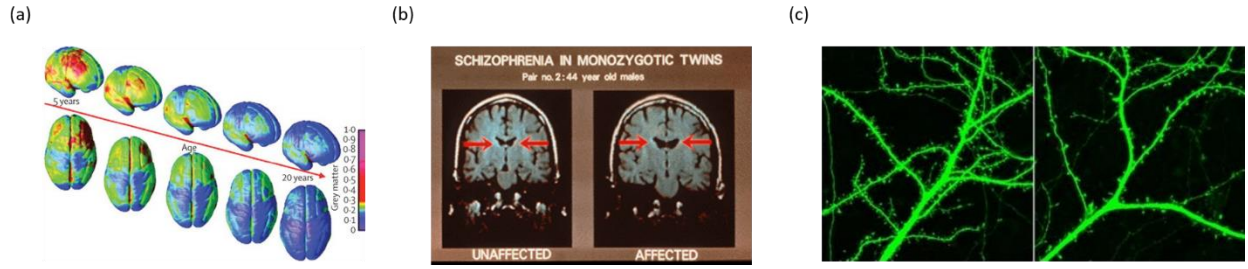


Figure 1|**Neuroanatomical abnormalities in schizophrenia**. **A**| Accelerated gray matter loss is present at first onset of schizophrenia symptoms in adolescence (Keshavan et al., 2014). **B**| Non-progressive ventricular enlargement (Dr. Daniel Weinberger, Clinical Brain Disorders Branch (NIH)). **C**| Pathological decrease in spine density (right) compared to healthy control (left) (Peter Penzes, Northwestern University Feinberg School of Medicine).

Dysregulated neurochemistry further complicates this condition. There are two hypotheses that have been widely studied and rather than compete with one another, they coexist in a complementation. The first of the two, the dopamine hypothesis, is in fact the oldest standing hypothesis in modern psychiatry. Chlorpromazine was initially discovered to be a highly effective antipsychotic drug in the early 1950s (Delay, Deniker, & Harl, 1952). It wasn't until a little over a decade later when the dopamine receptor blocking mechanism was elucidated (Carlsson & Lindqvist, 1963). Drugs known to be dopamine-enhancers, such as

cocaine and amphetamines, have been shown to produce psychosis-like behaviours as well (Brady, Lydiard, Malcolm, & Ballenger, 1991; Morton & Stock, 2000). The second hypothesis is the glutamate hypothesis. The first hint in support of this emerged when psychoactive phenylcyclidine was demonstrated to noncompetitively antagonise the NMDA receptor (NMDAR) in the central nervous system of cats (Lodge & Anis, 1982). It wasn't until five years later when a group formally reviewed the evidence and proposed the glutamate hypothesis of schizophrenia (Javitt, 1987). Ever since, evidence has only accumulated, showing that NMDAR agonists can reduce clinical symptoms (Coyle, 1996) while NMDAR antagonists produce positive symptoms (Wu et al., 2016).

It would be naïve to assume dopaminergic and glutamatergic pathways coexist independently, and so many unifying models have been proposed for the two hypothesis (Georg Winterer & Daniel R. Weinberger, 2004). Many of these theories converge at insufficient GABAergic activity and suggest a consequent lack of inhibition in schizophrenia. Both, the glutamatergic and dopaminergic pathways crosstalk with inhibitor interneurons, constantly receiving feedback in an effort to modulate their activity. In the glutamate hypothesis, cortical pyramidal neurons are required to activate inhibitory interneurons in order to produce an output that balances excitation and inhibition. In the event of NMDAR hypofunction, there is insufficient activation of inhibitory neurons and this results in disinhibition and consequently hyper excitability of cortical circuitry (Gordon, 2010). With regards to the dopamine hypothesis, the relationship between GABA and dopamine has been suspect in schizophrenia for quite some time now (Garbutt & van Kammen, 1983) and the effects of antipsychotic dopamine

antagonizing drug, clozapine, has been reported to be mediated through a dopamine-mediated GABA modulation (Mrzljak et al., 1996).

A number of mechanisms that contribute to manifestation of schizophrenia have been described. Whether all of these contribute equally in all the reported cases of schizophrenia, it is hard to say. However, two functional abnormalities are of particular interest. First, the signal to noise ratio (SNR) has been reported to be profoundly reduced in schizophrenia affected individuals (Loh, Rolls, & Deco, 2007; E. T. Rolls & Deco, 2011; G. Winterer & D. R. Weinberger, 2004; Winterer et al., 2000). Current ideas suggests that this is caused by dopamine dysregulation in conjunction with NMDAR and GABA hypofunction result in reduced stability of spontaneous states and increase of noise in the network (E. T. Rolls & Deco, 2011; Georg Winterer & Daniel R. Weinberger, 2004). The second phenomenon involves the abnormal activation of certain neuronal circuits, often to an exaggerated extent in regions such as the prefrontal cortex and sensory association cortices (Colon-Perez et al., 2016; Dierks et al., 1999; Juszczak, 2016; Okun et al., 2015; Shergill, Brammer, Williams, Murray, & McGuire, 2000; Weinberger et al., 2001). There is an increasing body of evidence that supports the idea that these abnormal patterns of activation reflect deficits in inhibitory mechanisms which allow the manifestation of hallucinations through excessive activation of memory traces and intrusion of thoughts into the consciousness (Juszczak, 2016; Smucny, Olincy, Eichman, Lyons, & Tregellas, 2013; Waters et al., 2012).

Schizophrenia is a complex psychopathology that is affected by a variety of underlying abnormalities. Neuroanatomical reductions in connectivity are partly supported by reductions in adolescent grey matter density, ventricular enlargement and decline in spine densities.

Neurochemical dysregulations are driven by dopaminegic hyper function and NMDAR hypofunction, which influence downstream GABAergic activity. Together these contribute to compromised synaptic architecture and imbalances in neurotransmission that result in widespread hyper excitability, abnormal patterns of activation and a profound reduction in signal to noise reduction.

## 3| Computational Models

The brain is a circuit, a complex network of interactions that, to this day, continues to puzzle the brightest minds in neuroscience. Fortunately, the technological revolution that we have seen emerge over the past few decades has done wonders for science. Computational models have become increasingly common. Given an appropriate framework and suitable parameters, complex biological systems can be reduced to a simple model that, if properly constructed, can recapitulate the behaviour of the system and on occasion provide further insight which can then be verified experimentally. Many models have been proposed to simulate hallucinations in silico. Three very different approaches will be discussed here to acquire an intuition for how the phenomenon can be modeled.

### 3.1 Previous Models

#### Disconnection Models

During adolescence the brain undergoes a phase of stabilization by eliminating inefficient and unused synapses in order to optimize the neuronal network's efficiency (Crews, He, & Hodge, 2007). The disconnection model argues that normally this pruning process predominantly targets redundant synapses. However, in the event of schizophrenia, this

elimination process is dysregulated and begins eliminating essential synapses in the neural network (McGlashan & Hoffman, 2000).

Simulations of a progressive Darwinian elimination model has demonstrated that excessive pruning, beyond 80% of synapses, results in spontaneous hallucinations (Figure 2, McGlashan & Hoffman, 2000). The Darwinian rule simply ensures that the weakest synapses are eliminated while the strongest persist. Amongst its strengths, this theory is consistent with the notion that schizophrenia is a neurodevelopmental disorder that arises early in life and helps explain how reduced synaptic connectivity can manifest as hallucinations.

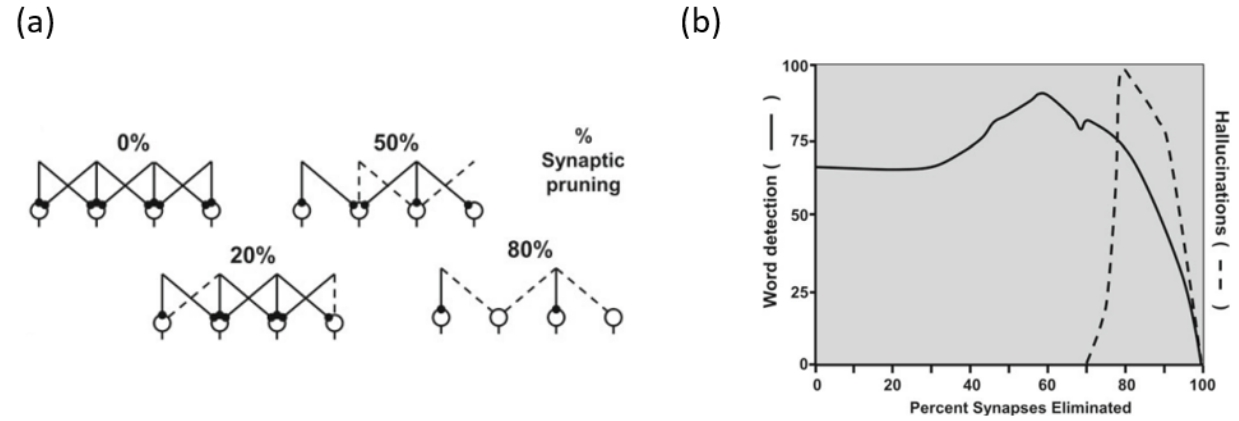


Figure 2| **Disconnectivity model for hallucinations**. **A**| Progressive Darwinian elimination of redundant synapses in the network. **B**| Synaptic pruning optimizes neuronal performance until as certain point when the pruning becomes excessive and results in hallucinations. (McGlashan & Hoffman, 2000)

Bayesian Prediction Models

Hypotheses that take root in signal detection theory propose that all information detection and processing occurs with a certain degree of uncertainty and that this sense of uncertainty is pathological in individuals with schizophrenia (Waters et al., 2012). These models adopt a Bayesian backbone and attempt to generate a probabilistic prediction of the sensory input given a set of previous observations and expectations. Hallucinations are then simulated by producing a certain threshold of prediction error which causes the network to oscillate between two states of states of belief, essentially emulating sensory-expectation contradictions (Figure 3, Deneve, 2008).

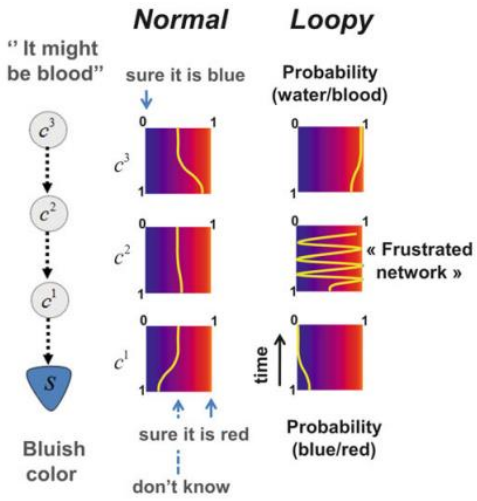


Figure 3| **Belief propagation using a Bayesian framework** (Deneve, 2008).

Integrate-fire attractor network

Assume an energy landscape, populated with basins of attraction, all of which represent potential energy states and, by extension, the stability of any given combination of neuronal activation patterns. Using the capacitance and leakage resistance of the cell membrane to model a neuron (Stein, 1967), an integrate-and-fire network can be constructed (Figure 4a), in which the stability of different activation patterns can be visualized by a given position on its respective energy landscape. If a memory trace or perception is represented by a basin of attraction, and the stability of that state is dictated by the depth of the basin, an integrate-fire attractor network can recapitulate the activity of a network with varying degrees of stability.

It has been proposed that reductions in cortical SNR that lead to network instability can be modeled by flattening these attraction basins in the energy landscape (Figure 4b). Consequently, any stochastic noise could cause spontaneously jumps between energy states, contributing to the instability of the network and seemingly random changes in perceptual states (Edmund T. Rolls, Loh, Deco, & Winterer, 2008).

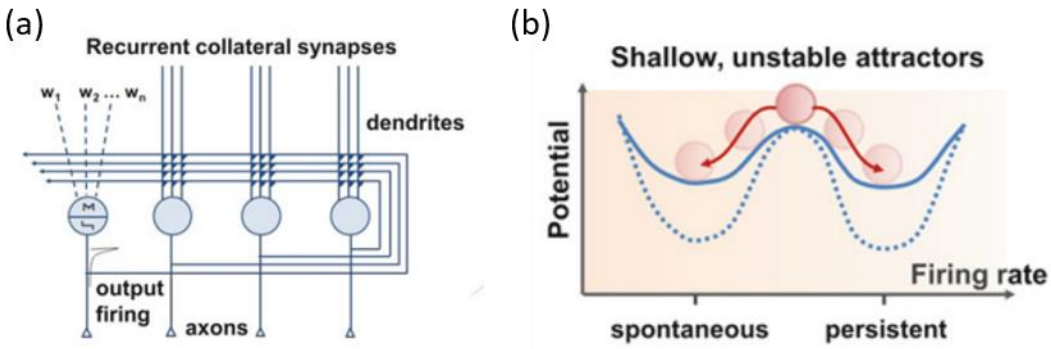


Figure 4| **A integrate and fire attractor state framework to model hallucinations**. **A**| Schematic representation of integrate and fire network. **B**| Flattening of energy landscape permits internal representations to move freely between different energy states.

## 3.2 Choosing a Model

The idea of using basins of attractions to model the stability of a network is a particularly appealing one as it has been previously adopted in modeling hallucinations. In order to implement such an approach, a network construct where each state of the network can be quantified through some energy function is required. Hence, if a state converges to a local minimum of the energy function, it will be considered a stable state of the network. However, if it fails to converge, and moves between energy states intermittently, the network can be deemed instable. Based on these characteristics, hallucinations can be artificially induced through the flattening of an energy landscape and destabilization of the network state.

Let us consider the Hopfield network which was first described by John Hopfield as a model for content addressable memory (Hopfield, 1982). The network is constructed by N nodes that are all defined by a binary state, $s_i$ (eq. 1), and form weighted connections,$w$, with one another. These connections are symmetric (eq. 2) and allow no self-feedback (eq. 3). Upon presentation of a biased pattern in the initial state (eq. 4), the network will asynchronously update the states of the nodes (eq. 5) until the network converges to a locally minimal energy state.

$$s_i = sign\left[\sum_{i=1}^{N} w_{ij} s_i\right] \quad \text{(eq. 1)}$$

$$w_{ij} = w_{ji} \quad \text{(eq. 2)}$$

$$w_{ii} = 0 \quad \text{(eq. 3)}$$

$$\bar{s}_{initial} = \bar{s}_{random} + (\theta \cdot p_j) \quad \text{(eq. 4)}$$

$$s_j(t+1) = sign \sum_{i=1}^{N} w_{ij} s_i(t) \quad \text{(eq. 5)}$$

The energy state of such a network is described by the Lyaponuv function where the energy of any state, $E(\bar{s})$, is dependent on the states, $s$, of connected nodes and the connection's weight, $w_{ji}$ (eq. 6).

$$E(\bar{s}) = -\frac{1}{2} \sum_{j=1}^{N} \sum_{i=1}^{N} w_{ji} s_j s_i \quad \text{(eq. 6)}$$

Training such a network involves storing patterns so that they represent basins of attraction, or minimal energy states. A weight matrix for a set of trained patterns, x, can be obtained through a Hebbian learning rule (Hebb, 1949).

$$w_{ij} = \frac{1}{N} x_i x_j \quad \text{(eq. 7)}$$

Hence, by this definition alone, the state of the Hopfield network can be describe by an energy function and the networks output is a stored pattern which can represent an internal representation of perception or memory allowing for an easier readout of hallucinatory states.

Next, the network must be capable of recapitulating aspects of schizophrenia in silico. Recall that dysregulated dopamine, NMDAR and GABA all contribute to a reduction in SNR in affected patients. Further, the decline in neuronal connectivity has been described to compromise synaptic architecture and lead to network instabilities. In order to reconcile these biological criteria with a reduction of depth of the attraction basins, we must convince ourselves that the flattening of an energy landscape is probabilistically equivalent to reducing the signal to noise ratio in the network.

Here is the rationale. If movement between energy states requires a certain energy threshold to be exceeded by the network, then reducing the depth of an attraction basin will lower this threshold. Alternatively, if the depth of the attraction basin remains the same, but the noise in the system is dramatically increased, the network will readily fluctuate to energy states that exceed the threshold. Hence, the network will readily enter some intermediate transitionary state before declining into another state elsewhere on the energy landscape. Therefore, for all intuitive purposes, reduction of the basin depth can be considered equivalent to a reduction in SNR. And to our convenience, we can model this using a Hopfield network.

### 3.3 Constructing the Model

To implement a Hopfield network susceptible to hallucinatory behaviour, two modifications to the network framework must be done. Traditionally, a Hopfield network

assumes some distorted pattern as an input, and it iterates until it converges to what is deemed the most energetically favorable state based on its trained repertoire of patterns. However, in the case of hallucinations, they manifest spontaneously. Therefore, rather than starting with a biased random state (eq. 4), the modified Hopfield network will start in a completely random state (eq. 8) to emulate a resting neuronal state that is not actively attempting to recall a memory.

$$\bar{s}_{initial} = \bar{s}_{random} \quad \text{(eq. 8)}$$

The second modification requires the introduction of varying degrees of noise into the network. This can be accomplished by introducing Gaussian white noise, $agwn$ (Matlab syntax), with each iteration, $t$, during pattern recall to simulate spontaneous neuronal discharges with varying levels of signal to noise ratio, $SNR$ (eq. 9).

$$s_j(t+1) = sign \sum_{i=1}^{N} \left( w_{ij} (s_i(t) \cdot agwn(SNR)) \right) \quad \text{(eq. 9)}$$

Taken together, this modified Hopfield network should be capable of starting at a random initial state and iterate in the presence of added Gaussian white noise until it either (1) converges to a stable state or (2) remains in a highly dynamic state of instability, moving between different energy states indefinitely.

## 4| Simulations

### 4.1 Network Architecture and Parameters

A simple network architecture is chosen to run the simulations. The modified Hopfield network is comprised of 15 nodes, $N$, and 3 stored patterns, $p$. Each time the simulation is run,

a set of 3 stored patterns is randomly generated and entrained so the weighting matrix and energy landscape of the network will vary between trials (Figure 5ab). The length of the each simulation, $t$, was set to 500 iterations.

SNR were chosen for healthy and pathological networks within previously described ranges (Hoffman, Quinlan, Mazure, & McGlashan, 2001; Edmund T. Rolls et al., 2008; Winterer et al., 2004). Normal networks were assigned a SNR of 10, while pathological networks were assigned a SNR of 1 (Figure 5c).

For the purpose of this discussion, healthy and normal will be used interchangeably, as will schizophrenia and pathological.

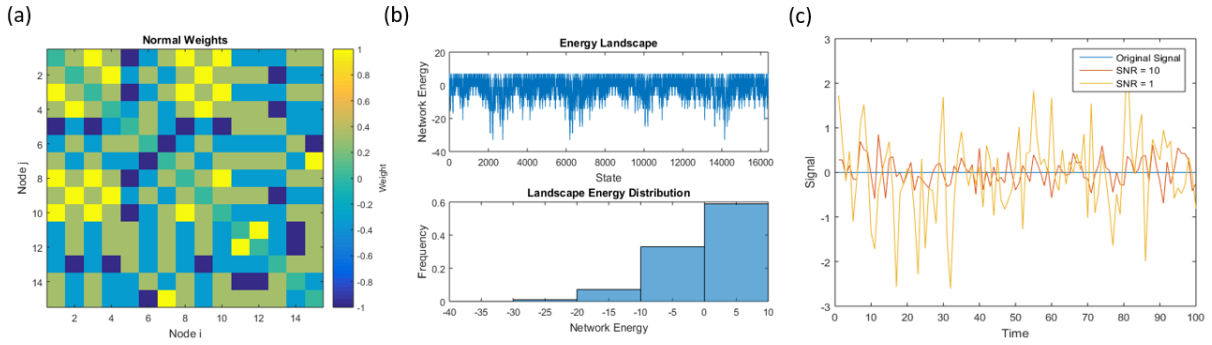


Figure 5| **Modified Hopfield network properties**. **A**| Typical weight matrix for a network entrained with randomly generated patterns. **B**| Typical Energy landscape (top) and distribution of energy states (bottom) for Hopfield network. **C**| White Gaussian noise is introduced to reduce the SNR of the network.

## 4.2 Excitability of Network

To understand how this modified Hopfield network behaves, the node activity was investigated over the span of the simulations (Figure 6). Although the mean number of nodes active at any given iteration is consistent for both, the normal ($51.6 \pm 1.2\%$ active nodes at given iteration) and pathological state ($50.2 \pm 9.1\%$ active nodes at given iteration), the

variance reveals certain instability in the pathological network (Figure 6a). The individual traces for the active nodes over time for a given sample trial reveal that the pathological network activity drastically fluctuates (Figure 6b). In contrast, the normal network activity remains consistent without the stochastic fluctuations seen in the pathological network (Figure 6b).

It was uncertain whether the nodes being stochastically turned on and off in the pathological network were the same nodes each time, or whether inactivation of nodes led to subsequent activation of a different subset of nodes. The trials were analysed to determine which proportion of the nodes in the network were activated at least once over the course of a 500 iteration simulation. Analysis of 50 trials reveals that the pathological network is seen to have a more widespread activation of unique nodes over the course of these simulations ($95.6 \pm 7.9\%$ of total nodes activated at least once), as opposed to the normal network which is seen to have a much lower proportion of unique node activation ($64.3 \pm 13.5\%$ of total nodes activated at least once) (Figure 6cd).

4.3 Hallucinatory Behaviour

To evaluate the recall of internally stored patterns in this resting state network, a measure of overlap of the network state with the stored patterns is used. Overlap here is defined as the dot product between the state matrix, $\bar{s}$, of the network and each training pattern matrix, $\bar{p}$ (eq. 10). Complete pattern recall or convergence is defined as 100% overlap.

$$overlap = \bar{s} \cdot \frac{\bar{p}}{N} \quad \text{(eq. 10)}$$

For the given network architecture, 4 outcomes were defined: (1) network does not converge to any stored pattern, (2) network converges to only 1 pattern, (3) network converges to exactly 2 patterns, (4) network converges to all 3 stored patterns within the span of the

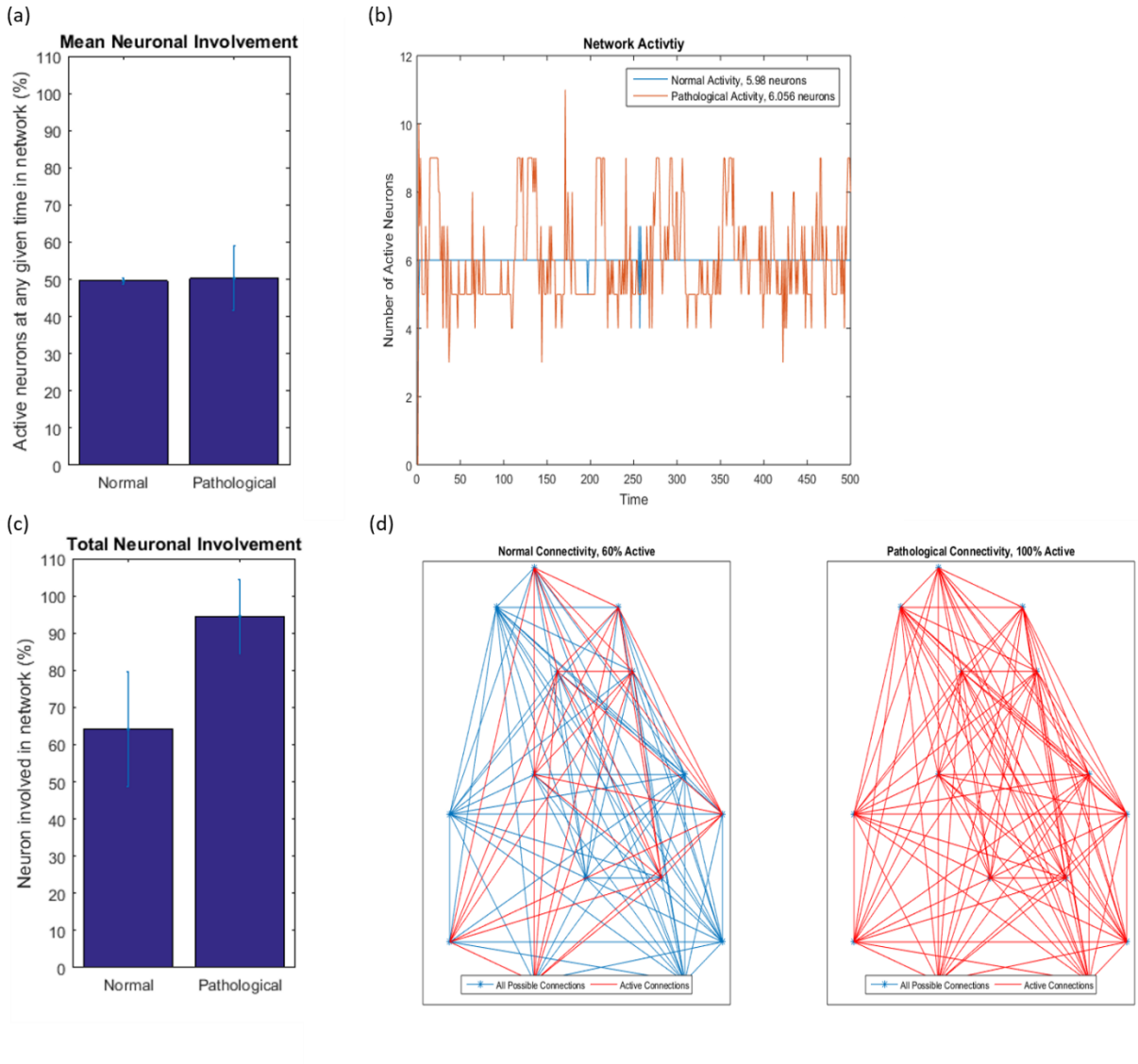


Figure 6| **Excitability of the Normal and Pathological Modified Hopfield Network**. **A**| Mean number of neurons active in the network at any given iteration (50 trials). **B**| Typical trace of neuronal activity over the course of a 500 iteration simulation. **C**| Percentage of neurons that were activated at least once over course of a 500 iteration simulation (50 trials). **D**| Typical node involvement over the course of an entire simulation.

simulation. For each simulation, the outcomes were recorded and summarized after 50 trials (Figure 7). In the normal network, there are two predominant outcomes, (1) no convergence to a stored pattern or (2) convergence to a single pattern. Notice that no convergence is slightly favored (56% of trials) over convergence to a single pattern (42% of trials) (Figure 7ab). In contrast, the pathological network routinely converges to either two or all three stored patterns over the course of the 500 iteration simulation (36% and 38% of trials, respectively), and rarely results in a no convergence or single pattern convergence outcome (4% and 12%, respectively) (Figure 7ac).

## 5| Discussion

Network hyper excitability and abnormal patterns of activation have been widely reported in cases of schizophrenia (Colon-Perez et al., 2016; Dierks et al., 1999; Juszczak, 2016; Okun et al., 2015; Shergill et al., 2000; Weinberger et al., 2001). The modified Hopfield network here has demonstrated reduced SNR does not result in the excess activation of neurons at any given time. Instead, different patterns in the network are stochastically activated over the span of the simulation leading to a more widespread cumulative involvement of the neurons (Figure 6cd). These results support previous findings that abnormal patterns of activation are present in schizophrenia networks. This abnormal activation and consequently recruitment of more neurons over a span of time may serve as an explanation for abnormal downstream consumption of energy within the system. In fact, there have been reports of patients with schizophrenia presenting increased levels of phosphocreatine and adenosine triphosphate concentrations, suggesting there is higher metabolic activity in these

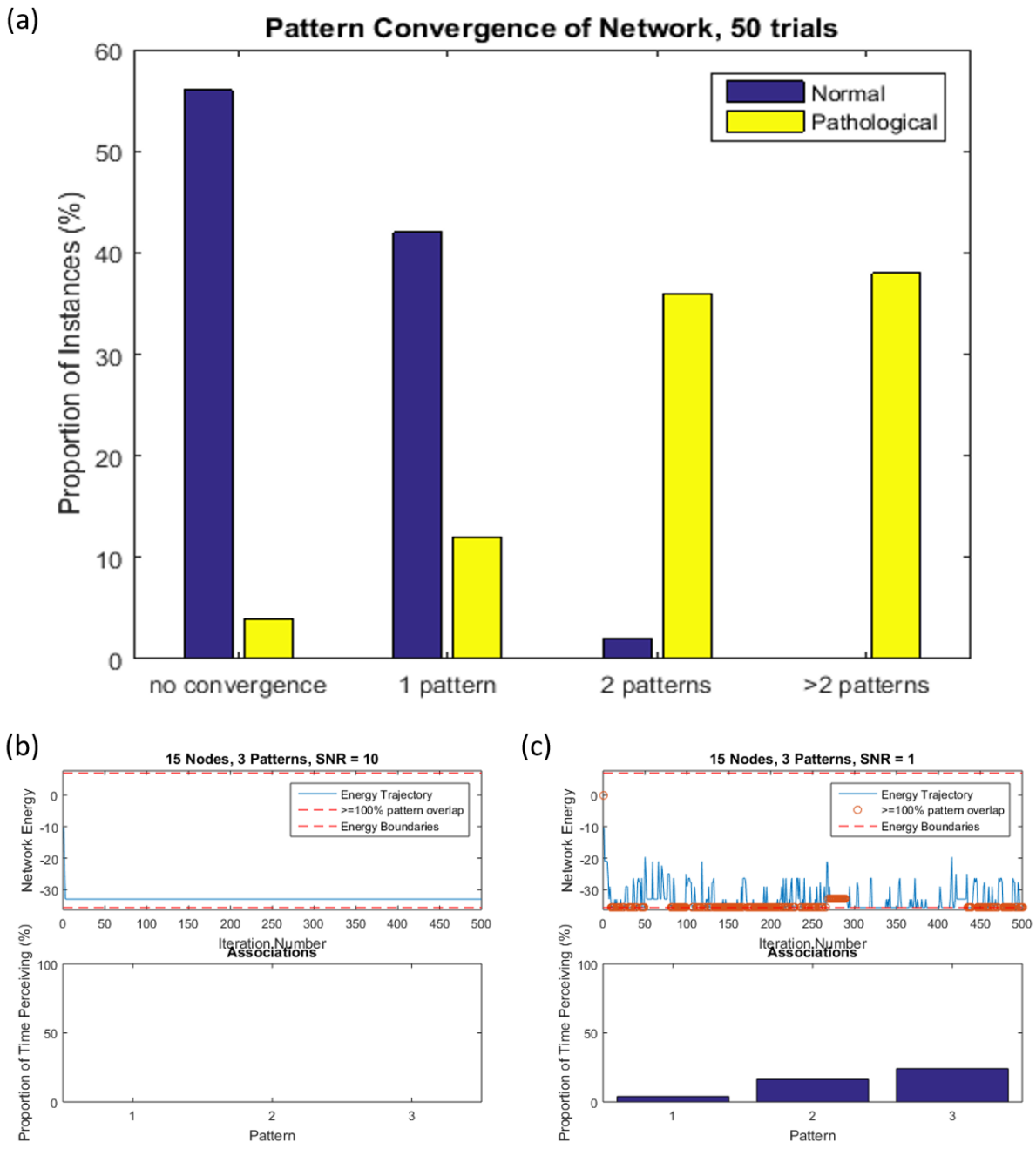


Figure 7| **Behaviour of modified Hopfield network in pattern recall at resting state**. **A**| Distribution of convergence outcomes for normal and pathological network (50 trials). **B**| Typical non-convergence outcome for normal network simulation. **C**| Typical three pattern convergence for pathological network simulation. Energy state for each iteration (top) and proportion of iterations in which a stored pattern is recalled (bottom) reflect the network stability throughout the simulation.

patients (Jensen et al., 2004). Similarly, another group has demonstrated that greater neural activity is accumulated in mesolimbic regions during auditory hallucinations using FDG-PET to monitor neuronal metabolism (Horga et al., 2014). Together, this evidence supports the hypothesis that there is excessive energy consumption in the schizophrenic brain due to abnormal network activation and inefficiency. This will require further experimental support in the future.

The pattern recall behaviour of the modified Hopfield network is of particular interest. Assuming a healthy amount of noise in the network (SNR = 10), simulations consistently result in either (1) no convergence or (2) very steady convergence to a single stored pattern (Figure 7a). In the case of no convergence, this can be interpreted as a situation in which the neural network is simply idling at a resting state, and no thoughts, perceptions or memory traces are brought forth into the consciousness. Alternatively, in the case of stable convergence to a single pattern, this can be conceptualized as an instance in which some internal representation is brought forth into the consciousness as a thought or perception. It is important to contrast even these single convergence states in the normal and pathological network. In a normal network, an internal pattern will be recalled stably without subsequent dramatic changes in the network state. This suggests stability in the perception. The pathological network on the other hand may spontaneously recall an internal pattern, but this is often a very transient convergence, and the noise in the system will tend to destabilize the converged state and cause the network into higher unstable energy states. It is for this reason, the pathological network is seen to frequently converge to two or three patterns throughout the simulation, which can therefore be interpreted as hallucinatory behaviour (Figure 7ac).

Taken together, if analogous attractor networks are present within the nervous system, the pathological reduction of SNR through disrupted connectivity and dysregulated neurochemistry effectively reduces the barriers to traversing an energy landscape. This may serve to explain how hyper excitability and spontaneous activation of internally stored states contribute to the manifestation of hallucinations in individuals affected by schizophrenia.

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