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A proposed tandem mechanism for memory storage in neurons involving magnetite and prions

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ABSTRACT

Knowledge about how information is stored in neurons of animals and in the human brain is still incomplete. A hypothesis related to long-term changes in synaptic efficiency has strong experimental support, but does not seem to be able to explain all observations. It has recently been proposed that magnetite together with a prion-like protein could be involved in a tandem mechanism for storage of memory in neurons in which electric impulses are received and reshaped by the magnetite to a form which can be accepted by the protein. The magnetite crystals can be magnetized by an electrical impulse, but they cannot hold the magnetism, which drops to zero after each impulse. Therefore, magnetite cannot be the substance in which information is stored. In the present paper we explain how a tandem mechanism could function in a neuron in which magnetite is situated together with a prion-like protein close to the cell surface membrane of the axon. We assume in addition that the information is stored in special *storage neurons.* With this, we propose a new hypothesis for information storage in neurons which could operate in addition to synaptic plasticity, but perhaps in different neurons.

Introduction

Knowledge of the mechanisms for storage of memory in neurons is incomplete. A hypothesis related to long-term changes in synaptic strength and the growth of new synaptic connections has strong experimental support [1]. A recent article [2] proposes the supplementary hypothesis that there are neurons in which a combination of magnetite and prion-like proteins (or prions for short) are involved in a tandem-mechanism in which the magnetite amplifies and reshapes electrical pulses to a form that can be accepted by the protein. An extension of this hypothesis is that there are special neurons in which this tandem-mechanism takes place. In this paper, we will discuss such an extended tandem-hypothesis and explain how we think a tandem-mechanism may function in such neurons. More specifically, an extension of this hypothesis is that there are neurons in which such proteins store the information, while the magnetite is needed to amplify electrical signals so that they can switch the protein between its two possible shapes, a ground state or initial condition, and a transformed state in which the neuron stores one bit of information. We will in this paper explain how we think the tandem-mechanism may function in neurons.

Prions have the crucial property that they can change shape from a normal resting form to an alternate chain-formed version. For brevity, we refer to a prion in the normal form as being in the *ground state*, and to one in the alternate form as being in the *excited state*. In [3] it is explained how a prion can be switched from the ground state to the excited state by an intricate *prion-chain reaction* triggered by an electric impulse.

It has also previously been proposed that magnetite is involved in the storage of information in neurons [4,5]. Magnetite is an iron oxide (Fe_3O_4) which is widely found in living organisms without being involved in any known biochemical reactions.

Electron microscopy has indicated the presence of a minimum of 5 million single-domain magnetite crystals per gram in human brain tissue. Black strings of aggregated particles can be extracted from brain tissue and can be viewed under low power through an optical dissecting microscope. The crystals range in size between 10 and 70 nm in diameter [6]. Magnetite crystals have also been found in bacteria and fish, where they were seen to be organized in membrane-bound chains with up to 80 single-domain crystals per chain [7,8]. Such chains appear to be present across all animal species.

The particles in these chains are magnetite crystals that are different from those formed through geological processes. The morphology of magnetite particles in living organisms is in fact particularly well suited for information storage in neurons because they have the crucial

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property that they can easily be magnetized by electrical impulses, but cannot hold the magnetism, which very quickly drops to zero after each impulse. Therefore, magnetite cannot be the substance in which information is stored. However, it is conceivable that information can nevertheless be stored in a neuron by means of a prion-chain reaction which switches prion in a neuron from the ground state to the excited state, whereby one bit of information will be stored in the neuron. In this process, electrical pulses driven by action potentials along a pathway of axons are magnetizing a chain of magnetite crystals. In this paper, we will present a version of the tandem hypothesis in which such a chain is located in the initial segment of an axon immediately downstream from where the action potential is generated.

However, it has recently been suggested that magnetite chains together with prions could be involved in a tandem mechanism in which incident electric impulses are received and reshaped by the magnetite, giving it a form that can be accepted by a prion in which the information can be permanently stored. This magnetite crystal should be located in the initial segment of the axon immediately downstream from where action potentials are generated,

In this paper we will explain how such a mechanism may function in a neuron where a nanocrystalline magnetite chain is located together with a prion close to the cell surface membrane, and how the electric impulses could trigger prion-chain reactions such that the information is stored in the prion.

A storage cell hypothesis

Nerve impulses (action potentials) are all-or-none electrical signals that encode neural information for long-distance communication along nerve fibers (axons). Action potentials have large, fixed amplitudes (about 100 mV), short durations (about 1 ms) and travel through long axons at speeds that range from below 1 to above 100 m s^{-1}, depending on the axon diameter and degree of myelination.

Action potentials are elicited if the membrane potential is depolarized to a threshold level. The threshold is lowest in the initial segment of the axon. After an action potential is generated at this site, it can spread without decay down the axon and all of its branches, and may (although with signal decay) also invade the cell body and proximal dendrites. Graded transmembrane potentials show exponential decay with distance from the generation site in the neuron, but multiple small potentials may summate so that the threshold is reached and an action potential is fired in the initial segment of the axon, even if each input is too small to reach the threshold alone.

The transmembrane ionic currents associated with the passage of a propagated action potential (an inward Na^+ current through voltage-gated sodium channels, and, after a brief delay, an outward K^+ current through voltage-gated potassium channels) will generate a local rotating current that could potentially magnetize a properly oriented rod of magnetite nanocrystals, as we explain here. We propose a tandem mechanism by which the propagation of an action potential in an axon could, given that specific conditions are satisfied, magnetize a local rod of magnetite nanocrystals that in turn could change the conformation of a local prion and store a permanent memory of the event.

How can electrical signals magnetize the magnetite chain?

According to the tandem hypothesis, information is stored in a special type of neurons, called *storage neurons*, which contain one and only one magnetite chain together with a prion that can be in one of two possible states.

In a storage neuron, the bursts of Na^+ ions into the cell and K^+ ions out of the cell create vortices that rotate on their axes like short-lived electrical currents. When such vortices rotate around a magnetite chain, they can magnetize it. These vortices arise when two oppositely directed flows of ions pass through neighboring membrane areas. If P1 and P2 are sufficiently close ion channels, the two flows will interact and produce vortices that rotate clockwise in the (x-z)-plane (Fig. 1).

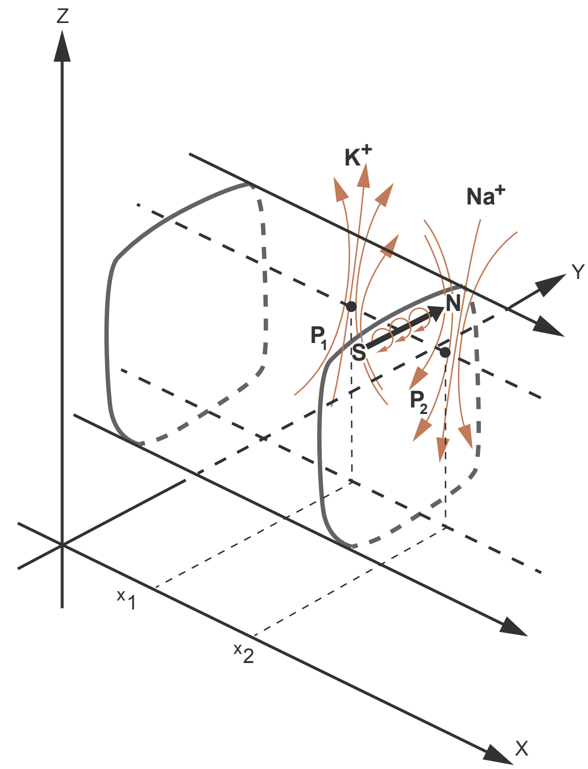

Fig. 1. Two oppositely directed bursts of ions through neighboring ion channels can create vortices that magnetize the magnetite chain in a storage neutron. The action potential travels along the cell surface membrane in the x-direction. The sodium channels are open near point P_2 and the potassium channels near point P_1. The magnetite chain S-N is located laterally close to the cell membrane and oriented in the y-direction.

According to this argument, incident signals in a storage neuron can create vortices of short-lasting electrical currents that rotate like a whirlwind around the magnetite chain, and these currents can magnetize the chain. However, the magnetite chain differs from an electromagnet, as described below.

How can the magnetite chain change the shape of the prion?

We have seen that the magnetite chain in a storage neuron can be magnetized by currents rotating around it, but it is not so easy to explain how the magnetic chain can change the shape of the prion, since it requires an electric and not a magnetic impulse to do this. Here it may be helpful to use an analogy with a familiar electric device, a transformer, which sets up a pulsating electromagnetic field that produces eddy currents.

In the same way, when the magnetite chain of a storage neuron is magnetized by electric pulses, it will set up a pulsating electric field which produces ionic currents. These will rotate in right-handed vortices around the magnetized magnetite chain like a whirlwind. A detailed proof of this can be obtained by an elementary argument, but all we need to know here is that the electric field at a given point is largest close to the magnetized chain, and that it decreases rapidly with increasing distance from the chain.

Why is nanocrystalline magnetite particularly suited for the storage of information in neurons?

Magnetite (Fe_3O_4) is an iron oxide which differs from ordinary rust (Fe_2O_3) in its crystalline structure and its specific magnetic properties.