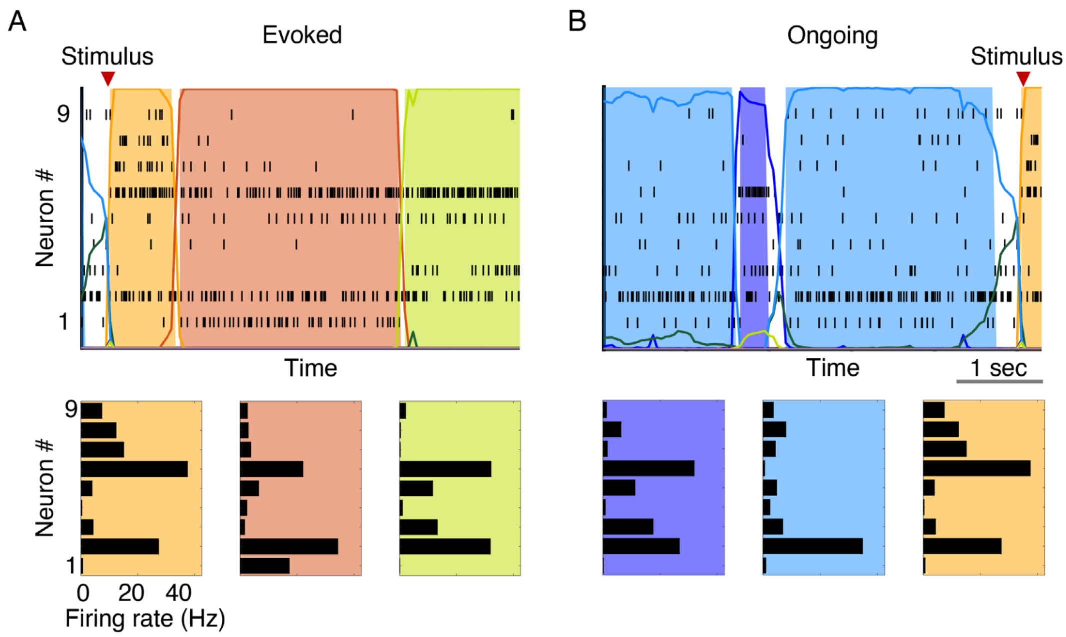

FIG. 1. Example of metastable neural dynamics. (a) Top panel: segmentation of neural activity from nine simultaneously recorded neurons in the rat gustatory cortex. Each line is a spike train, i.e., a sequence of spike times from one of the nine neurons. Recordings were taken as the animal waited and then received a tastant in its mouth at random times ("stimulus"). Colored areas correspond to hidden states of the neural activity, each color representing a different state. A bin of data was assigned to a state if the probability of being in that state, given the data, was higher than 0.8 (colored lines). Bottom panel: the hidden states can be represented as vectors of firing rates across the nine neurons. (b) Same as (a) for "ongoing" neural activity, i.e., for neural activity in the "idle time" between two stimuli. See Sec. V A 8 for details.

of finite size, these configurations become metastable, as shown in numerical simulations. This model has so far explained a wealth of data, mostly obtained in the GC of rodents, including the temporal modulation of transition rates due to expectation[8] as well as the reduced dimensionality of the neural activity evoked by a stimulus compared to ongoing activity.[22]

In this Review, we give a detailed and up-to-date description of metastability in cortical circuits together with current modeling efforts. We start from a definition of metastability in physics and neuroscience and with a clarification of the kind of metastability that is the main focus of this Review (Sec. II): the one characterized by repeatable metastable transitions, rather than metastability, en route to a ground state configuration. We exemplify this notion in a classical spin system in Sec. III. We then review evidence of metastable dynamics in neural circuits and describe how such metastable dynamics can explain important features of sensory and cognitive processes (Sec. IV). We then present statistical models of metastable dynamical systems and methods for their analysis with an emphasis on hidden state models (Sec. V A). This section is followed by a section on theoretical models of metastable dynamics (Sec. V B), proceeding from cortical networks of spiking neurons to more formal models interpretable as coarse-grained descriptions of population activity. Mean field reductions of these models are essential for understanding their behavior and typically result in firing rate models of spiking networks. We also present a path integral formalism for studying metastability in non-equilibrium systems lacking detailed balance, an approach known as the landscape and flux theory of neural networks.[23,24] Section VI will focus on the problem of learning and plasticity, specifically, how metastable circuits can be formed via experience-dependent plasticity and can sustain themselves in the face of ongoing metastable activity. We will review the available evidence for neural clusters and present a concrete example of the existing models focusing on this problem as well as theoretical investigations of the consequences of learning in models of memory, decision making, and fear expression. Finally, in Sec. VII, we summarize the main points reviewed in this article and appraise the potential role of metastable dynamics in neural coding and cortical computation in comparison to earlier views.

II. DEFINITIONS OF METASTABLE DYNAMICS

In physical systems, metastability typically refers to the long-lived occupation of a state with higher energy than the lowest energy state.[25,26] For simple biological and chemical systems, such as the case of isomerization, this definition also applies. The long time spent in the metastable state is due to the presence of effective energy barriers that prevent the system from easily making transitions to lower energy states. Thermal agitation or external perturbation can induce the system to escape the metastable state. In systems with many local energy minima, metastable dynamics may ensue as transitions among states with lower energy after some amount of lingering in each metastable state, eventually reaching the lowest energy state (potentially after an asymptotically long time).[27,28] It is possible, however, that there are many minima of comparable energy, and noise fluctuations may be able to knock the system between these different configurations repeatedly. More generally, any stochastic process in which many