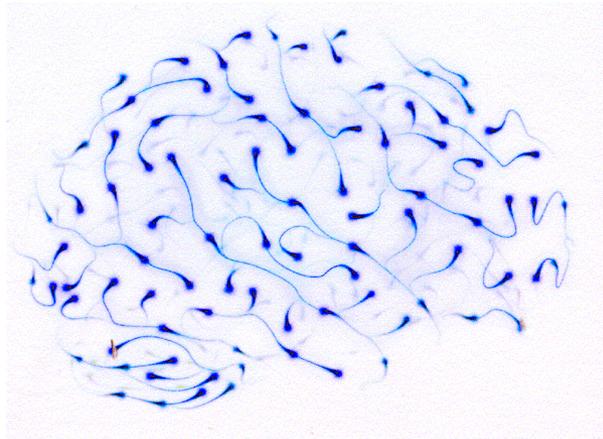
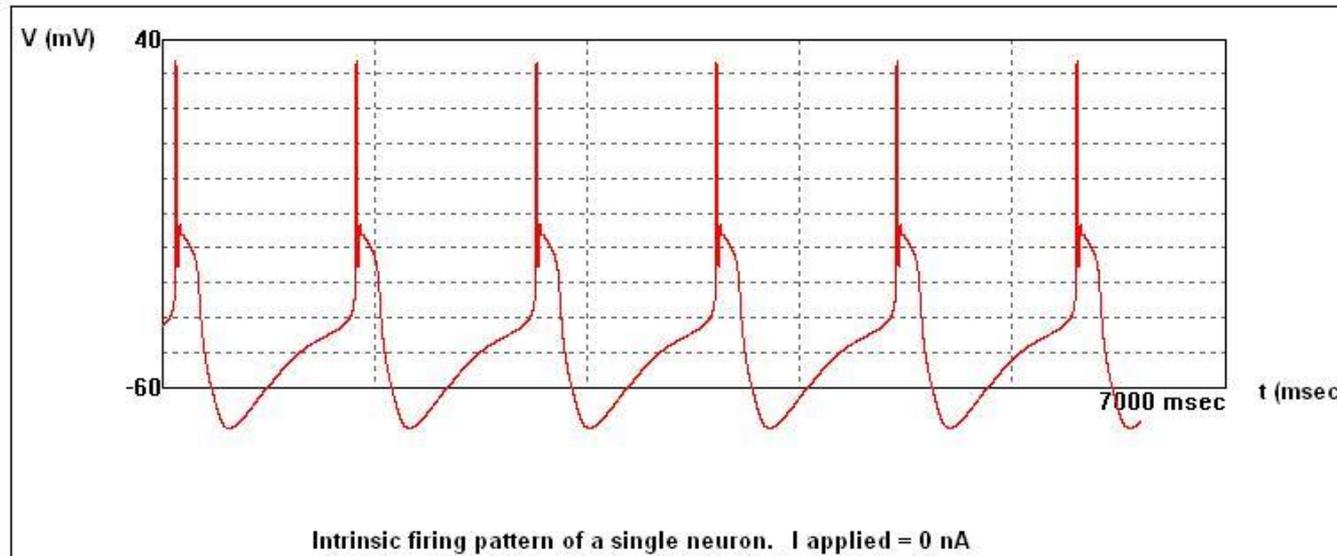


# Bursting dynamics in the brain



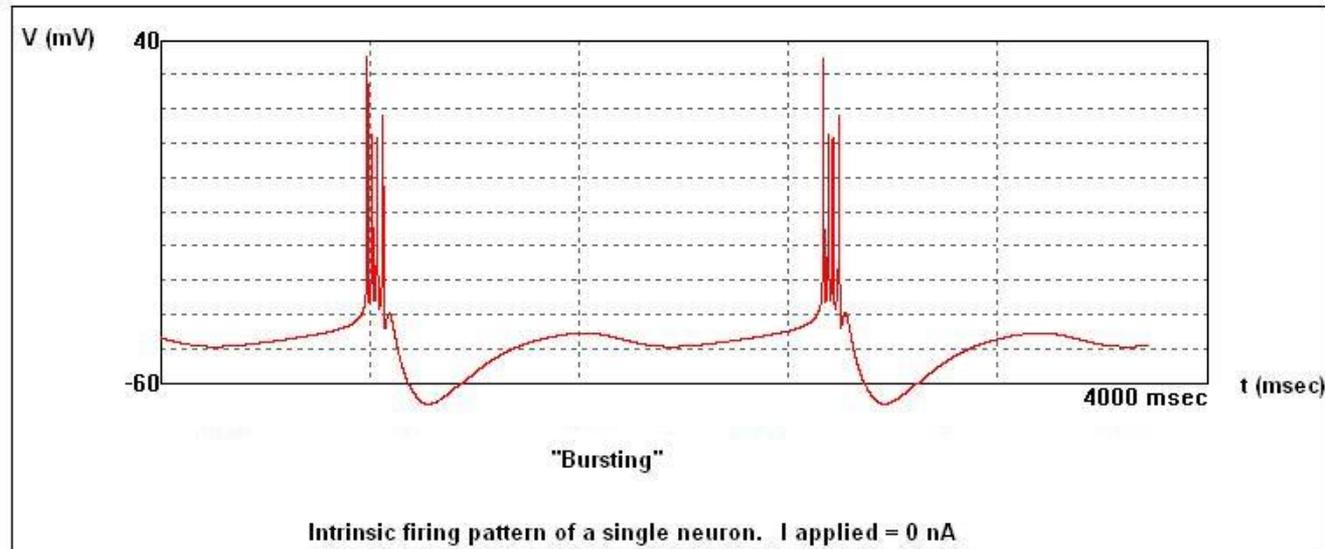
Jaeseung Jeong,  
Department of Biosystems,  
KAIST

# Tonic and phasic activity

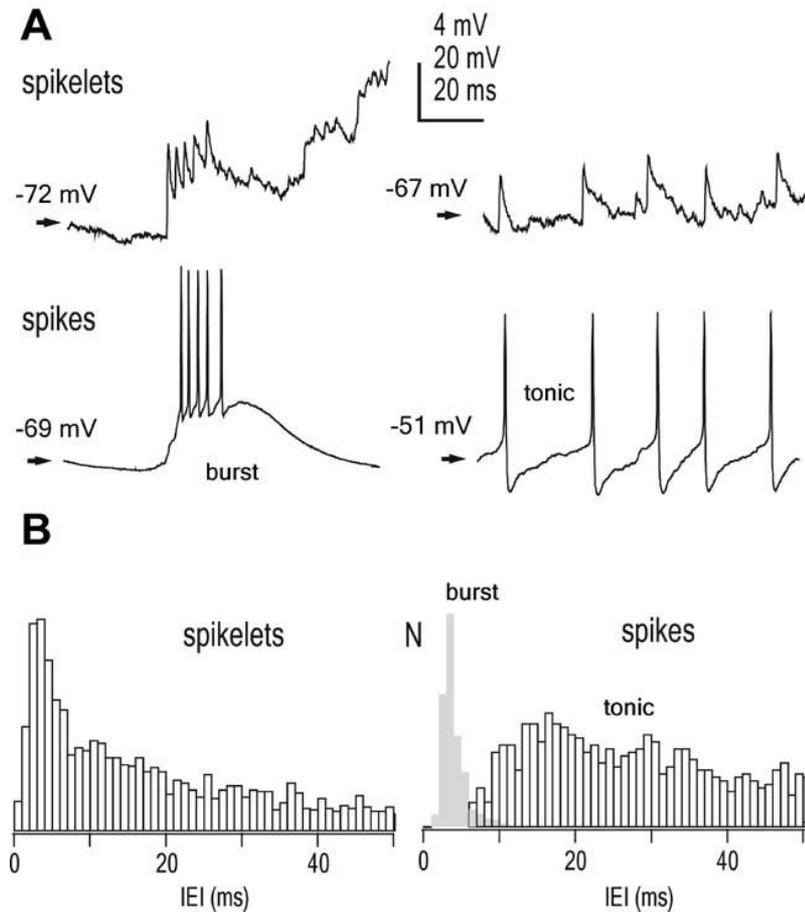


- A neuron is said to exhibit a tonic activity when it fires a series of single action potentials randomly.

# Tonic and **phasic** activity



- A neuron is said to fire a **burst** of spikes (**phasic activity**) when it fires two or more action potentials followed by a period of quiescence. A burst of two spikes is called a *doublet*, of three spikes is called a *triplet*, four - *quadruplet*, etc.



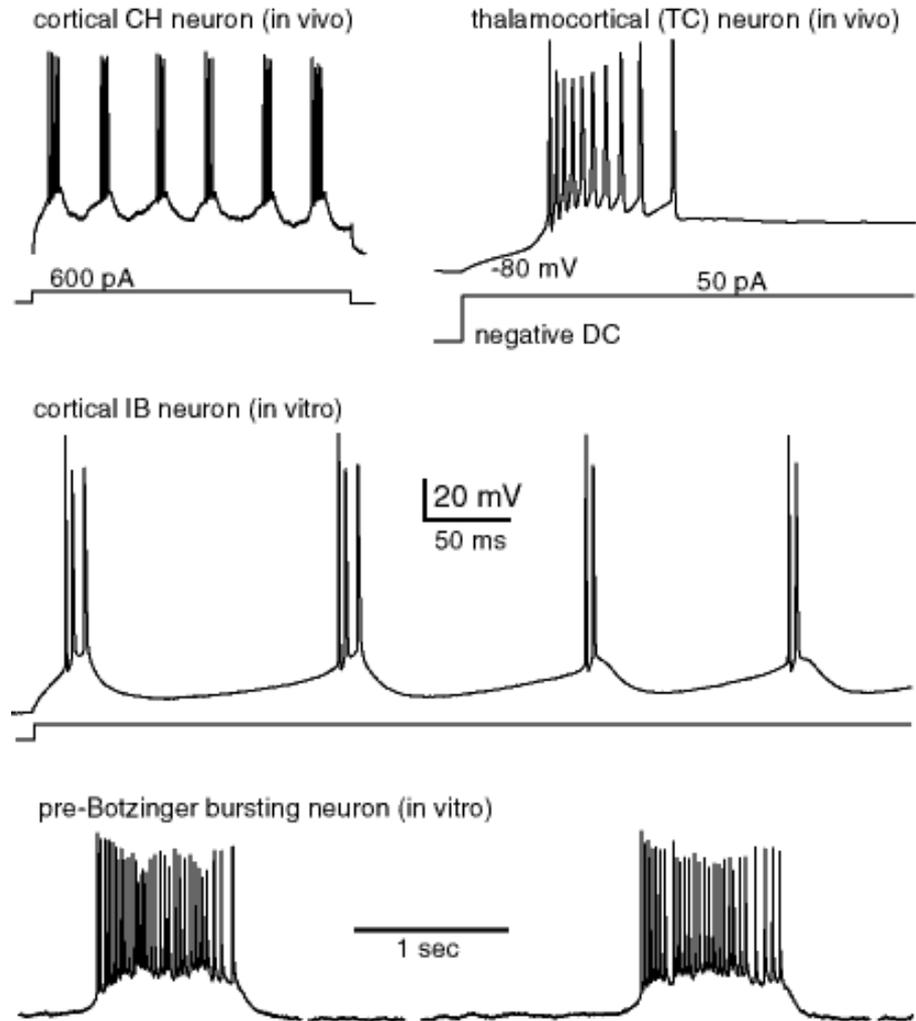
- Almost every neuron can burst if stimulated or manipulated pharmacologically.
- Many neurons burst autonomously due to the **interplay of fast ionic currents** responsible for spiking activity and **slower currents** that modulate the activity.

# Examples of bursting neurons

- **Neocortex**

IB: Intrinsically bursting neurons, if stimulated with a long pulse of dc current, fire an initial burst of spikes followed by shorter bursts, and then tonic spikes. These are predominantly pyramidal neurons in layer 5.

CH: Chattering neurons can fire high-frequency bursts of 3-5 spikes with a relatively short interburst period. Some call them fast rhythmic bursting (FRB) cells. These are pyramidal neurons in layer 2-4, mainly layer 3.

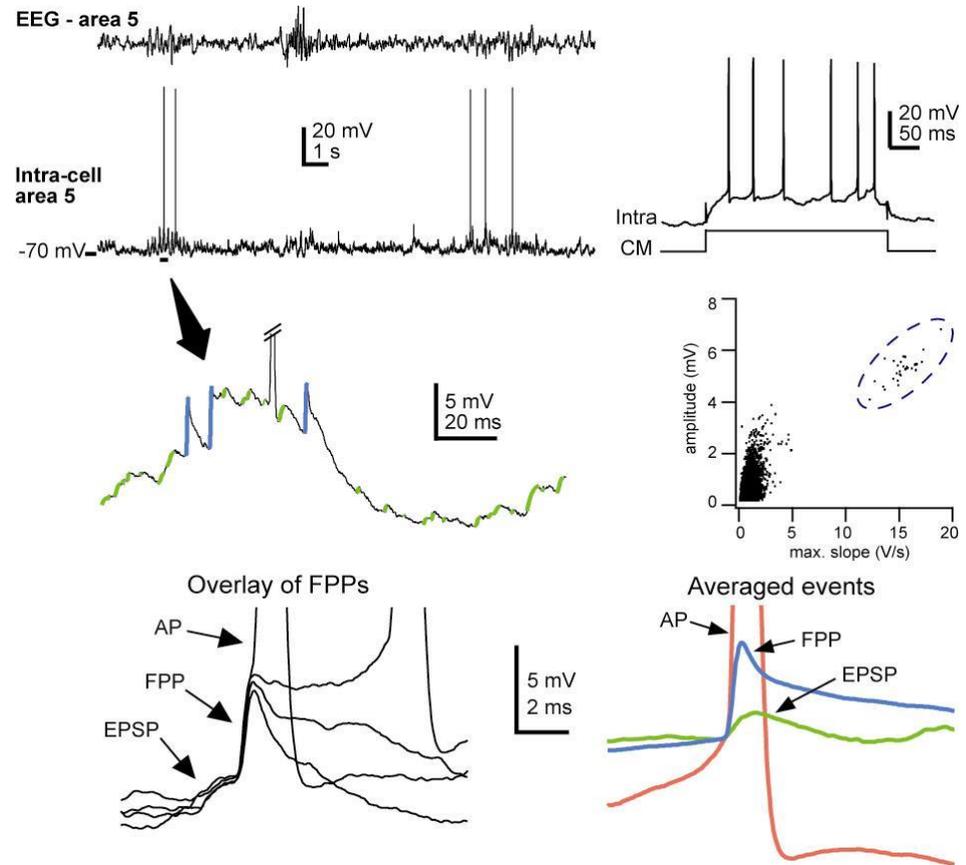


# Examples of bursting neurons

- **Hippocampus**

LTB: Low-threshold bursters fire high-frequency bursts in response to injected pulses of current. Some of these neurons burst spontaneously. These are pyramidal neurons in CA1 region.

HTB: High-threshold bursting neurons fire bursts only in response to strong long pulses of current. (fyi, fpp: fast prepotentials)

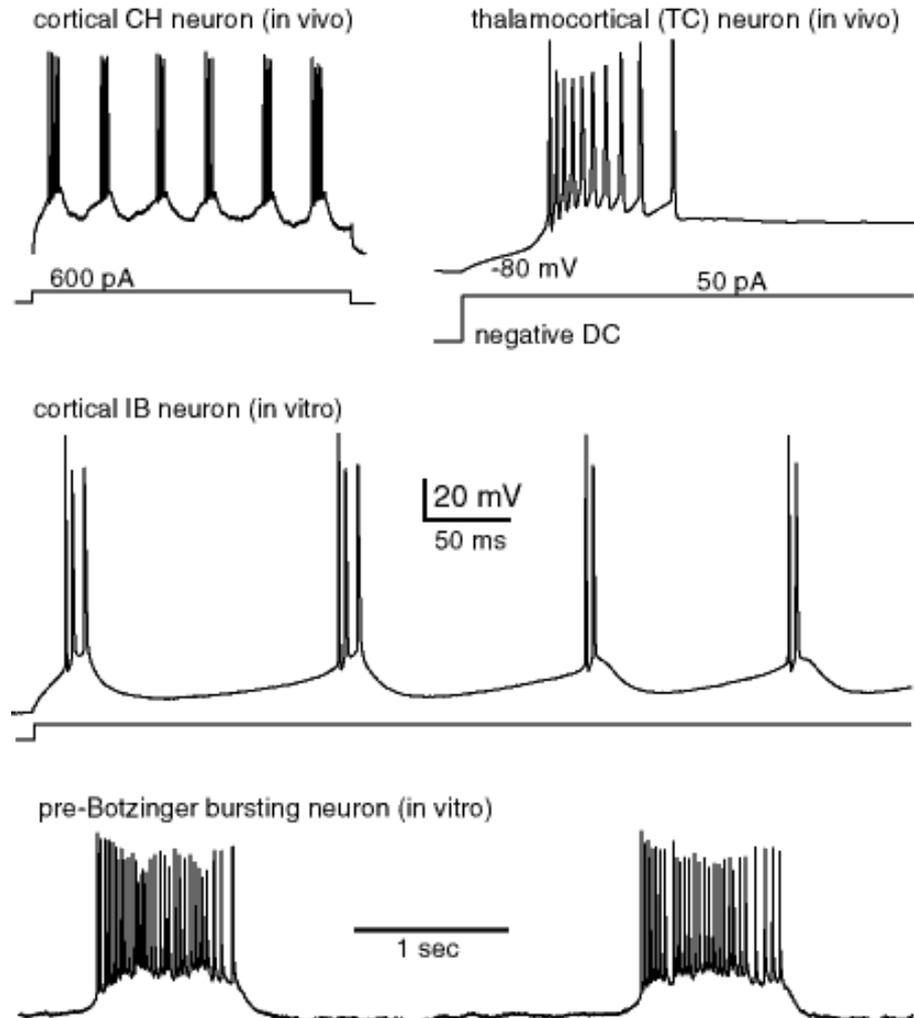


# Examples of bursting neurons

- **Thalamus**

TC: Thalamocortical neurons can fire bursts if inhibited and then released from inhibition. This rebound burst is often called **a low-threshold spike**. Some fire bursts spontaneously in response to tonic inhibition.

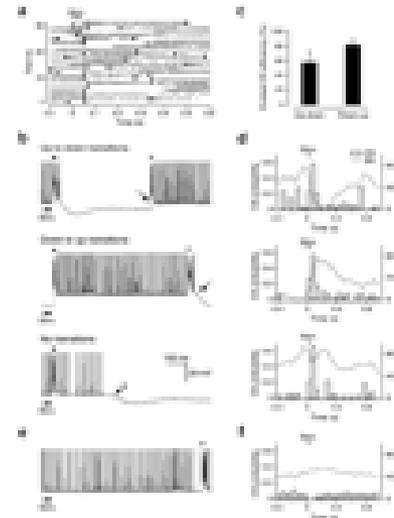
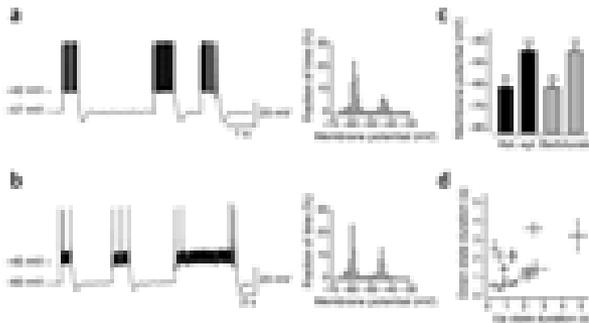
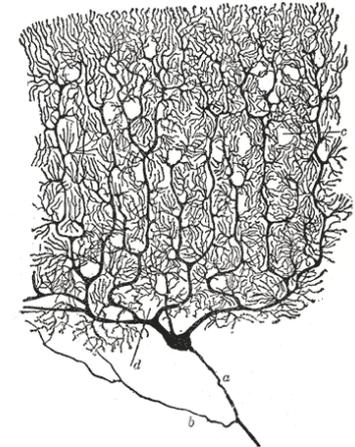
RTN: Reticular thalamic nucleus inhibitory neurons have bursting properties similar to those of TC cells.



# Examples of bursting neurons

- Cerebellum**

PC: Purkinje cells in cerebellar slices usually fire tonically but when synaptic input is blocked they can switch to a trimodal pattern which includes a bursting phase.



# Examples of bursting cells

- **Other structures**

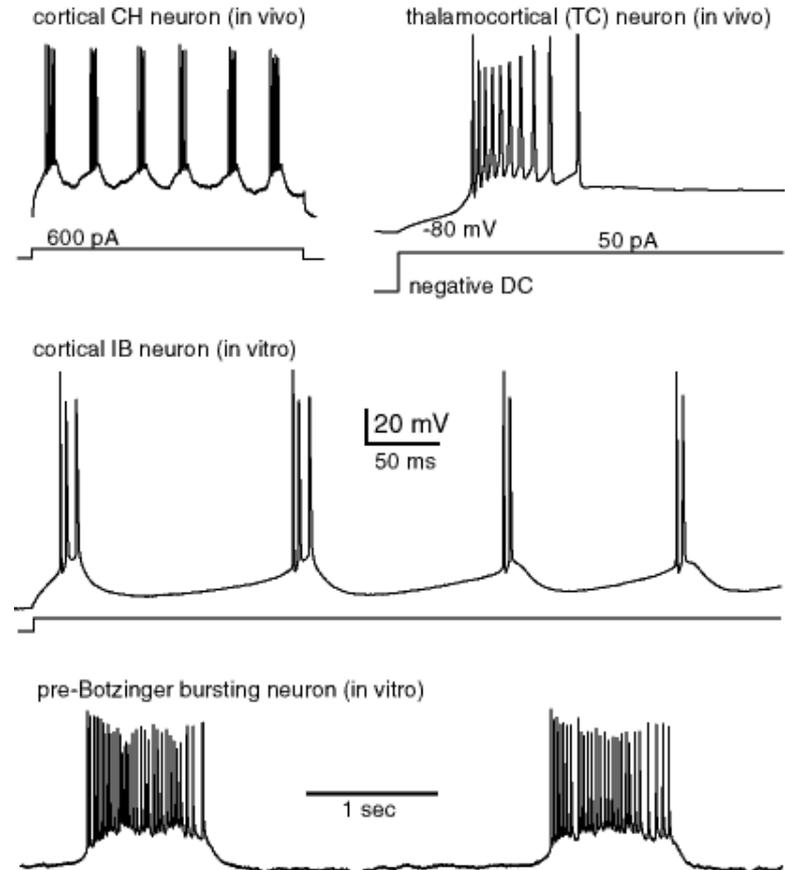
pre-Bot: Respiratory neurons in pre-Botzinger complex fire rhythmic bursts that control animal respiration cycle.

MesV: Some Mesencephalic V neurons in brainstem may fire rhythmic bursts when slightly depolarized above the threshold.

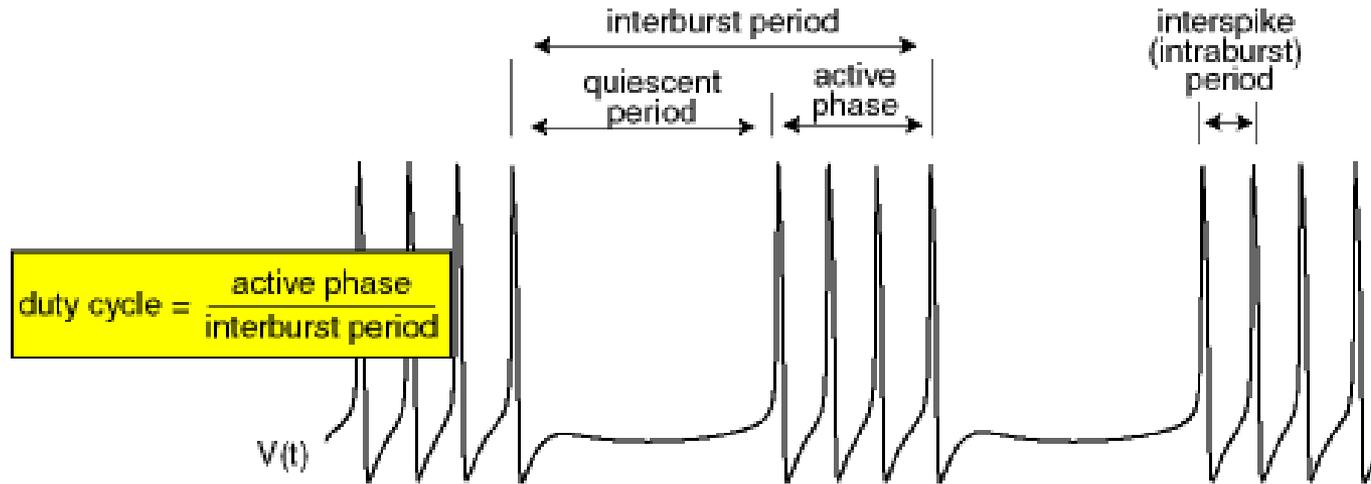
AB: Anterior bursting neuron in lobster stomatogastric ganglion fires rhythmic bursts autonomously.

R15: Aplysia abdominal ganglion neuron R15 fires autonomous rhythmic bursts.

$\beta$ -cell: Pancreatic  $\beta$ -cells fire rhythmic bursts that control the secretion of insulin.

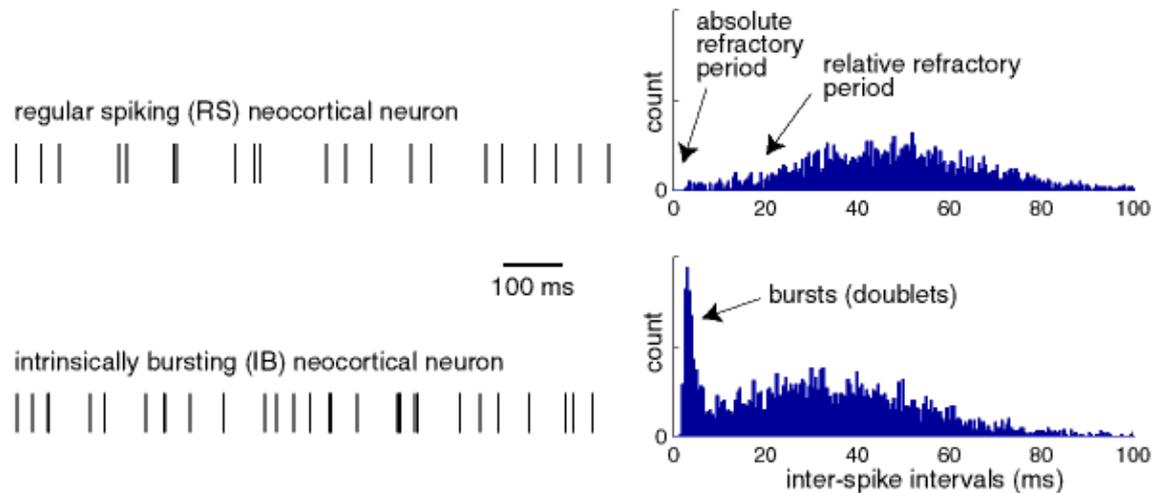


# Detection of bursts



- It is relatively easy to identify bursts in response to simple stimuli, such as dc steps or sine waves, especially if recording intracellularly from a quiet in vitro slice. The bursts fully evolve and the hallmarks of burst responses are clear.
- However, **responses to sensory stimuli** are often comprised of doublets or triplets embedded in spike trains. Furthermore, these responses are usually recorded extracellularly so the experimenter does not have access to the membrane potential fluctuations that are indicative of bursting. Thus, **it is difficult to distinguish burst responses from random multispikes events.**

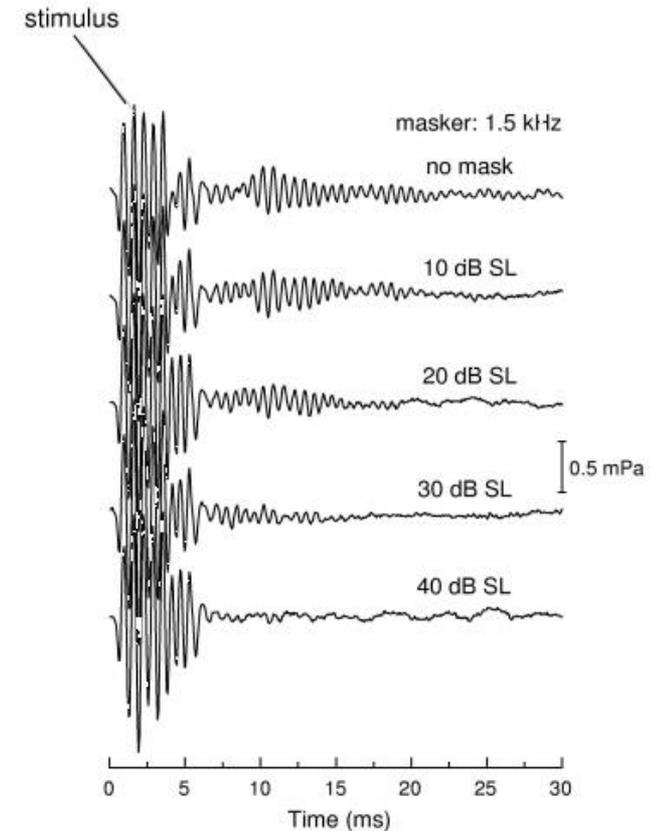
# The statistical analysis of bursting activity



- **Bimodal inter-spike interval (ISI)** histograms can be indicative of burst responses. The rationale is that short ISIs occur more frequently when induced by burst dynamics than would occur if predicted by Poisson firing. Burst spikes with short ISIs form the first mode while quiescent periods correspond to the longer ISIs of the second mode.
- This is true for intrinsic or forced (stimulus driven and network-induced) bursting. Furthermore, the trough between the two modes may correspond to the refractory period of an intrinsic burst or the timescale of the network-induced bursting.
- This method defines **a criterion for burst identification** so that further analysis and experimentation can determine the mechanism and function of the bursts.

# Bursts as a Unit of Neuronal Information

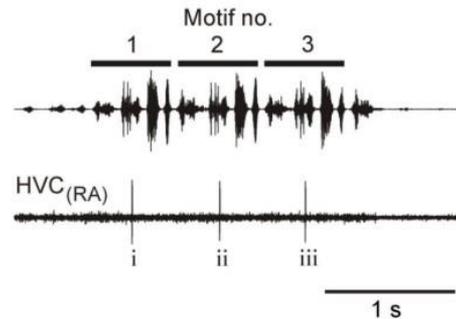
- Bursts are more reliable than single spikes in evoking responses in postsynaptic cells. Indeed, excitatory post-synaptic potentials (EPSP) from each spike in a burst add up and may result in a superthreshold EPSP.
- Bursts overcome synaptic transmission failure. Indeed, postsynaptic responses to a single presynaptic spike may fail (release does not occur), however in response to a bombardment of spikes, i.e., a burst, synaptic release is more likely.
- Bursts facilitate transmitter release whereas single spikes do not. A synapse with strong short-term facilitation would be insensitive to single spikes or even short bursts, but not to longer bursts. Each spike in the longer burst facilitates the synapse so the effect of the last few spikes may be quite strong.
- Bursts evoke long-term potentiation and hence affect synaptic plasticity much greater, or differently than single spikes (Lisman 1997).



# Bursts as a Unit of Neuronal Information

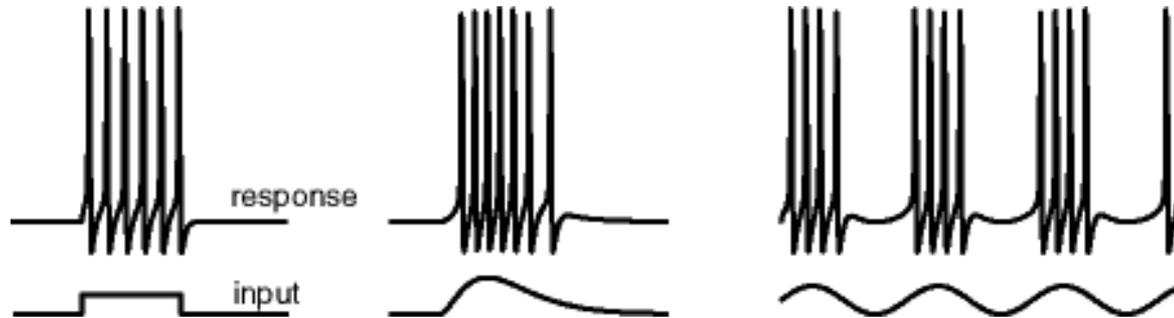
- Bursts have higher signal-to-noise ratio than single spikes. Burst threshold is higher than spike threshold, i.e., generation of bursts requires stronger inputs.
- Bursts can be used for selective communication if the postsynaptic cells have subthreshold oscillations of membrane potential. Such cells are sensitive to the frequency content of the input. Some bursts resonate with oscillations and elicit a response, others do not, depending on the interburst frequency.
- Bursts can resonate with short-term synaptic plasticity making a synapse a band-pass filter. A synapse having short-term facilitation and depression is most sensitive to a burst having certain resonant interspike frequency. Such a burst evokes just enough facilitation, but not too much depression, so its effect on the postsynaptic target is maximal.

# Bursts as a Unit of Neuronal Information



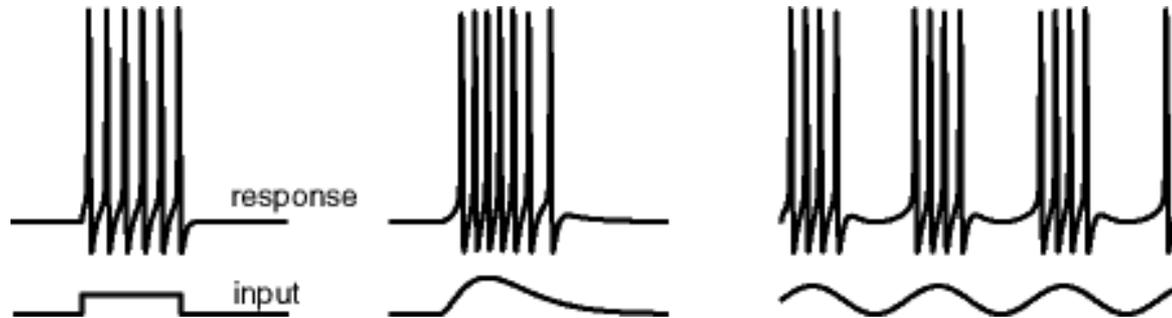
- Bursts encode different features of sensory input than single spikes. For example, neurons in the electrosensory lateral-line lobe (ELL) of weakly electric fish fire network induced-bursts in response to communication signals and single spikes in response to prey signals.
- Bursts have more informational content than single spikes when analyzed as unitary events. This information may be encoded into the burst duration or in the fine temporal structure of interspike intervals within a burst.
- **Burst input is more likely to have a stronger impact on the postsynaptic cell than single spike input,** so some believe that bursts are all-or-none events, whereas single spikes may be noise.

# Ionic mechanisms of forced burst generation



- Most spiking neurons can burst if stimulated with **a current that slowly drives the neuron above and below the firing threshold**. Such a current could be injected via an electrode or generated by the synaptic input.
- RA neurons in the songbird burst in response to drive from HVC neurons (neurons of the song premotor nucleus). The bursting arises as a result of either network dynamics within RA (robustus archistriatalis) or is inherited from HVC. The central role of **RA** is to map the temporal sequence onto particular acoustic patterns.
- Network induced bursts of electric fish. Here bursting arises because periodic

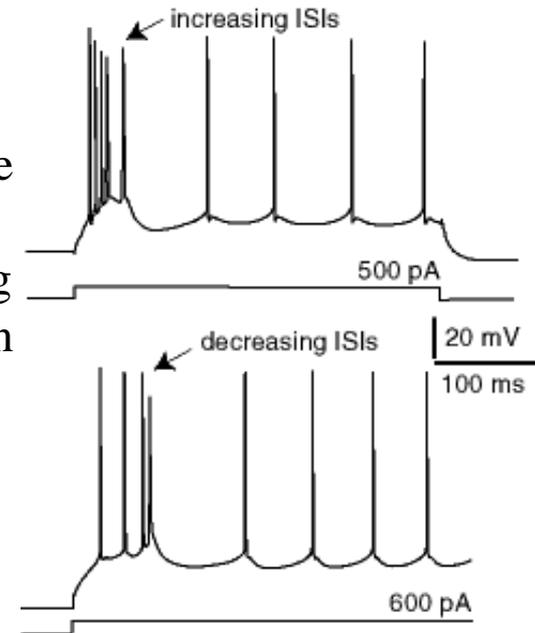
# Ionic mechanisms of intrinsic bursting generation



- Many neurons have **slow intrinsic membrane currents** that can modulate fast spiking activity. Typically, the currents build up during continuous spiking, hyperpolarize the cell and result in the termination of the spike train. While the cell is quiescent, the currents slowly decay, the cell recovers, and it is ready to fire another burst.
- Much experimental research is aimed at identifying these slow currents, so that bursting can be manipulated. To produce an inhibitory effect, i.e., to stop the burst, spiking activity should either
  - activate (turn on) an outward current, e.g., persistent  $K^+$  current, or
  - inactivate (turn off) an inward current, e.g., transient  $Ca^{2+}$  current.

# Ionic mechanisms of intrinsic bursting generation

- Neocortical pyramidal neurons exhibiting chattering activity have voltage-gated  $K^+$  M-current. Midbrain dopaminergic neurons have  $Ca^{2+}$ -gated  $K^+$  current  $KCa$ . In both cases, continuous spiking activates **the outward  $K^+$  currents** and results in burst termination.
- Thalamic relay neurons have voltage-gated  $Ca^{2+}$  T-current. Anterior bursting neurons in lobster stomatogastric ganglion have  $Ca^{2+}$ -gated  $Ca^{2+}$ -current, called L-current. In both cases, continuous spiking inactivates **the inward  $Ca^{2+}$  currents** resulting in burst termination. In these cases, the interspike intervals within the burst is typically increasing.
- Bursting can result from the **somatic-dendritic interplay**: Somatic spike excites dendritic tree resulting in a delayed spike there. Dendritic spike depolarizes the soma and evokes another somatic spike, which results in another dendritic spike etc. The interspike intervals of the burst is typically decreasing up to the point when a somatic spike falls into the refractory period of the dendritic spike, fails to evoke dendritic response, and stops the burst.



# Summary

1. Bursting DA neurons had nonlinear determinism in ISI firing patterns, whereas non-bursting DA neurons did not.
2. Burst time series extracted from bursting DA neurons showed nonlinear determinism, whereas single spike time series did not.
3. Inter-burst interval data of bursting neurons demonstrated nonlinear deterministic structure.

**These findings suggest that bursts are likely source of nonlinear determinism in the ISI data of DA neurons.**

Jeong et al. Bursting as a source of nonlinear determinism in temporal spiking patterns of nigral dopamine neurons. *J Neurophysiology* (revised)