# Introduction

Intrinsically bursting cells in PreBC believed to be source of respiratory rhythmogenesis. There are three classes of pattern in action potentials for pacemaker cells, bursting, quiescence (silence), and tonic spiking. Only bursting leads to/produces normal breathing behavior. Quiescence indicates a total lack of firing by a neuron and tonic spiking refers to firing of neurons at an approximately constant rate, neither of which are conducive to a breathing pattern capable of supporting life.

Two channels commonly believed to contribute to bursting behavior of preBotC neurons are Ca2+ current (thats the current, what is the channel called?) and persistent sodium current.

Inap causes voltage dependent frequency modulation, but the inclusion of the Ican component reduces the voltage dependence and leads to greater heterogeneity of burst and inter burst intervals across the voltage range.

Neurons in the preBC respond demonstrably when exposed to ATP []. The channels generating the response are the purinergic P2X and P2Y receptors [].

P2XR and P2YR are also believed to contribute to bursting behavior, more so P2YR, and specifically P2Y1, than P2X. However, while [] found that intrinsic bursting continues despite blocking of P2X channels and therefore could not be directly responsible for intrinsic bursting, they were unable to rule out P2XRs and a contributor to bursting behavior.

Simulations of biological systems can be a useful alternative to costly and time-consuming ‘wet-lab’ experiments (technical term?). At best, such simulations are only as accurate as the mathematical model describing the system. The complexity of biological systems often prohibits detailed models, leading to the use of approximations such as the Hodgkin-Huxley formalism. An additional concern is the addition of realistic noise, as models are highly deterministic without it. Having said that, simulations can still be helpful in approximating system behaviors and test models of systems for accuracy by comparison with real data. Despite these flaws, computational models can make estimates of behavior, and can be used to test the validity of a mathematical description of a system by comparison of model data with experimental data.

The model is based on the Hodgkin-Huxley formalism, where neuron membranes are described as circuits with ion channels represented by resistors in parallel with a parallel capacitor (borrow image from The Hodgin-Huxley Model.pdf?). The voltage changes in accordance to the function,

$\frac{dV}{dt} = \frac{1}{C} \left( \sum\limits\_{ion} I\_{ion} - I\_{ext} \right) $. In [], BRS added a persistent sodium current $I\_{NaP}$ and in [], TB added a dendritic calcium current $I\_{CaN}$.

Several sources [][][] note neural excitation due to ATP in the preBC, which is generally attributed to the P2 purinergic receptors. According to [], the primary source of this excitation is P2YR, however, P2XR play a role, but perhaps not a pivotal one [Funk paper?].

While the presence of P2X7 in neurons is widely disbelieved, multiple sources [][][] acknowledge that it cannot be ruled out altogether.

Although P2X2 and P2X5 are potential P2XRs from the lit, we hope to locate P2X7 in neurons of the preBC (personal conversation) in future experiments (can I give any reason we think P2X7Rs are in neurons of the preBC? ‘Because my PI said so’ isn’t a very professional reason…).

We define the model in Python, and solve them using odeint, the ordinary differential equation integrator function found in Scipy, an open-source scientific-computing library written in Python\* (see index/attached .py file for code).

[] has claimed that P2X doesn’t have a significant effect on burst frequency. Several models describe the P2X current for a single channel on the order of pico amps or tens of pico amps\*, so we expect P2X to make a small contribution to the whole cell current\*, particularly if the number of channels on neurons must be small enough to so frequently escape detection. This should result in a modest effect on the membrane voltage, possibly slightly depolarizing the cell, but should result in little to no change in burst frequency, and therefore have marginal possible effect on breathing rhythm.

————Notes and Crap————

If we add a P2X component and it changes frequency in a noticeable way, either the model is wrong or P2XR does not occur in neurons of preBotC.

\*could not find data about how many receptors are on a neuron for any of the P2X7 receptors

(note: probably picoAmps or tens of picoAmps worth, although it may actually be a single channel current, so the amount of current might increase) ionic current that will shift the eL necessary for busting to (either lower or higher values…)

Indeed, an additional voltage independent current would make the model even less voltage independent

each message per million message per million reads = ~10 thousand receptors

10th-100thou receptors

# Methods