**Respiratory model**

Based on paper by Alona Ben-Tal and Jeff Smith, **Control of breathing: Two types of delays studied in an integrated model of the respiratory system.** *Respiratory Physiology & Neurobiology* 170, 103–112, 2010.

**Diaphragm**

**Pleural**

**cavity**

**Lungs**

**Brain stem**

**O**

**∫**

**Rhythm**

**generator**

**Pattern**

**generator**

**gas exchange**

**Blood**

**Gas exchange**

**Pleural
cavity**

**Diaphragm**

**pre-BӧtC**

**VRG**

*K*

**Model 1: Respiratory rhythm generation in the pre-Bӧtzinger complex**

The rhythm generator in the pre-Bӧtzinger complex (pre-BӧtC) produces an oscillatory output signal from a model containing two first order ODEs:

 (1)

 (2)

where is the open probability of the inactivation gate of a persistent sodium channel that controls the activation rate constant in eqn (1):

 ,

and s-1 is the maximum value of the rate constant. Note that the activation gate is kept at a quasi-steady state value dependent on feedback from :

 (; )

The inactivation rate constant and the external drive (which could be either inhibitory or excitatory) in eqn (1) are given by

 and

where 98 s-1 , 0.6667 (a scaling parameter), 0.212 is the recoil rate constant of muscle, and is a control parameter given by

 .

 13.2 s-1 is the nominal value of the control parameter and the other terms, scaled by A1 to D1, each represent a proportional (first two terms) or integral (second two terms) feedback process

 ;

based on the partial pressures of O2 and CO2, and , respectively, in the blood at the end of the alveolar capillary network. =104mmHg and =40mmHg are reference values for the blood partial pressures of O2 and CO2, respectively.=2.5mmHg.L-1 is the lung elastance. are parameters with the values shown in Table 1 for various types of feedback. is a function representing haemoglobin saturation.

**Variables for pre-Bӧtzinger model**

|  |  |
| --- | --- |
| **Symbol** | **Meaning** |
|  | output signal from pre-Bӧtzinger complex |
|  | open probability of the inactivation gate of a persistent sodium channel |
|  | activation rate constant |
|  | inactivation rate constant |
|  | external drive (inhibitory or excitatory) |
|  | activation gate |
|  | control parameter |
|  | feedback term for partial pressure of blood O2 |
|  | feedback term for partial pressure of blood CO2 |
|  | partial pressures of O2 in blood at the end of the alveolar capillary network |
|  | partial pressures of CO2 in blood at the end of the alveolar capillary network |

**Parameters for pre-Bӧtzinger model**

|  |  |  |  |
| --- | --- | --- | --- |
| **Symbol** | **Meaning** | **Value** | **Units** |
|  | activating rate constant of  | 133.33 | s-1 |
|  | inactivating rate constant of  | 98 | s-1 |
|  | parameter affecting  | 0.367 |  |
|  | parameter affecting  | -0.033 |  |
|  |  |  |  |
|  | scaling factor | 0.6667 |  |
|  | Recoil rate constant of muscle | 0.212 |  |
|  | case-dependent scaling factors | see table below |  |
|  | lung elastance | 2.5 | mmHg.L-1 |
|  | nominal value of the control parameter  | 13.2 | s-1 |
|  | reference value for the blood partial pressures of O2  |  |  |
|  | reference value for the blood partial pressures of CO2 |  |  |
|  |  |  |  |
|  |  |  |  |

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Case | A1 | B1 | C1 | D1 |
| 1 | 0 | 0 | 0 | 0 |
| 2 | 0 | 0 | 0 | 0 |
| 3 | 0 | 0 | 0 | 0 |
| 4 | 0 | 0 | 0 | 0 |
| 5 | 0 | 0 | 0 | 0 |
| 6 | 0 | 0 | 0.1 | 0 |
| 7 | 0 | 0 | 0 | 0 |

**Model 2: Inspiratory pattern generator in the ventral respiratory group**

The oscillatory output from the pre-Bӧtzinger complex drives the inspiratory pattern generator in the ventral respiratory group (VRG). The output from this model, , is the ramp signal that is sent to the phrenic nerve innervating the respiratory muscles. is obtained by integrating the signal numerically over one burst (see Ben-Tal and Smith, 2008 for more details). The model uses a leaky, resetting oscillator

where is a control parameter

dependent on the feedback functions

 and .

**Model 3: Diaphragm**

 is the displacement of the diaphragm in the downward direction, driven by the ramp signal in the phrenic nerve:

where =2 s-1 and = 103 s-1 are empirically determined parameters.

**Model 4: Pleural cavity**

The pleural pressure is driven down by the downward displacement of the diaphragm to suck air into the lungs

where =755.5 mmHg is a reference pressure and =2.5 mmHg.m-1 is the active stiffness.

**Airway mechanics**

The alveolar total pressure is given by

where =2.5 mmHg.L-1 is the lung elastance, =760 mmHg is the airway pressure at the mouth, and

Is the … …. is the air flow through the airways; and are the partial pressures of O2 in blood and alveolar air, respectively; and are the partial pressures of CO2 in blood and alveolar air, respectively; and the parameters =3.5x10-4 L.s-1.mmHg-1 and =7.08x10-3 L.s-1.mmHg-1 are the diffusion capacities of oxygen (1.56x10−5 mol.s−1.mmHg−1) and carbon dioxide (3.16 x10−5 mol.s−1.mmHg−1), respectively.

The partial pressure of O2 in blood must satisfy a flux balance in which the rate of increase in dissolved oxygen (, where =1.4x10-6 mol.L-1.mmHg-1 is the solubility of O2 in plasma) and haemoglobin-bound oxygen (, where is the saturation function for oxygen binding to haemoglobin and =2x10-3 mol.L-1 is the concentration of haemoglobin in blood) contained within the capillaries (volume =0.07 L) is equal to the flux of oxygen diffusing from the alveoli to the capillaries, driven by the pressure difference ():

or

or

**Model 5 Gas exchange**

 ;

|  |  |  |  |
| --- | --- | --- | --- |
| **Symbol** | **Meaning** | **Symbol** | **Meaning** |
|  | Concentration of O2 in alveoli |  | Partial pressure of O2 in blood at the end of the capillary |
|  | Concentration of CO2 in alveoli |  |  |
|  |  |  | Inspired concentration of O2 |
|  |  |  | Inspired concentration of CO2 |
|  |  concentration |  |  |
|  | Lung volume |  | Inspired air flow  |

**Model 6 Blood**