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A computational model of insect discontinuous gas exchange: A two-sensor, control systems approach

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HIGHLIGHTS

- We model insect respiration using interacting O_2 and CO_2/pH control systems.
- Realistic respiration patterns and pH and CO_2 fluctuations are generated.
- A prolonged open spiracle phase cannot be governed by a single pH threshold.
- Hysteresis in the CO_2/pH system is key to generating realistic model results.

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ABSTRACT

The insect gas exchange system is characterised by branching air-filled tubes (tracheae/tracheoles) and valve-like structures in their outer integument (spiracles) which allow for a periodic gas exchange pattern known as the discontinuous gas exchange cycle (DGC). The DGC facilitates the temporal decoupling of whole animal gas exchange from cellular respiration rates and may confer several physiological benefits, which are nevertheless highly controversial (primarily reduction of cellular oxidative damage and/or respiratory water saving). The intrinsic and extrinsic factors influencing DGCs are the focus of extensive ongoing research and little consensus has been reached on the evolutionary genesis or mechanistic costs and benefits of the pattern. Despite several hypotheses and much experimental and evolutionary biology research, a mechanistic physical model, which captures various key elements of the DGC pattern, is currently lacking. Here, we present a biologically realistic computational, two-sensor DGC model (pH/carbon dioxide and oxygen setpoints) for an Orthopteran gas exchange system, and show computationally for the first time that a control system of two interacting feedback loops is capable of generating a full DGC pattern with outputs which are physiologically realistic, quantitatively matching experimental results found in this taxonomic model elsewhere. A finite-element mathematical approach is employed and various trigger sets are considered. Parameter sensitivity analyses suggest that various aspects of insect DGC are adequately captured in this model. In particular, with physiologically relevant input parameters, the full DGC pattern is induced; and the phase durations, endotracheal carbon dioxide partial pressure ranges, and pH fluctuations which arise are physically realistic. The model results support the emergent property hypothesis for the existence of DGC, and indicate that asymmetric loading and off-loading (hysteresis) in one of the sensor feedback loops, which is a novel inclusion here, is a critical aspect of the insect spiracle-tracheal gas exchange system.

1. Introduction

Insects possess a gas exchange and respiratory system in which air-filled tubes lead from the outer integument, where there are spiracles as valves, and branch finally into smaller tracheoles, where gas exchange is thought to take place; tracheoles are fluid-filled at their tips but can penetrate close to mitochondria, where cell respiration and aerobic energy metabolism occur. This is significantly different from a vertebrate, mammalian gas exchange system in which there are lungs and a circulatory system with an oxygen carrier (haemoglobin), from which oxygen is delivered to tissues where cellular respiration takes place, again in mitochondria. This structural diversity gives rise to key functional physiological differences, most notably in the external gas exchange patterns—and specifically the discontinuous gas exchange cycle

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(DGC)—typically shown by several key insect groups (cockroaches, beetles, ants, butterfly pupae, and crickets and grasshoppers). Indeed, in at least five cases (or more, depending on the precise classification of DGC) DGCs are present in the derived physiological state (Marais et al., 2005; White et al., 2007), suggesting that the pattern confers some evolutionary fitness benefits.

The DGC consists of three phases: the closed or constricted phase (CP), in which the spiracles are sealed; the flutter phase (FP), in which the spiracles open and close rapidly; and the open phase (OP), in which the spiracles are fully open for an extended period. DGC is in contrast to continuous and cyclic ventilation, observed in the same insects under different ambient conditions or metabolic demands: hypercapnic and hypoxic environments both induce the abandonment of DGC in favour of continuous respiration; reduction in ambient oxygen levels typically results in an increased cycle frequency before DGC is abandoned (e.g. Terblanche et al., 2008; Chown and Holter, 2000). Experimentally induced increases in metabolic rate have both increased the cycle frequency, and in the extreme produced an open-spiracle state (e.g. Contreras and Bradley, 2009; Heinrich and Bradley, 2014).

There is much speculation and debate on the reasons for the occurrence of the DGC pattern, in terms of its mechanisms as well as its role in the overall physiological functioning of the insect. Contreras et al. (2014) provide a recent comprehensive review, highlighting again the distinction between adaptive and non-adaptive hypotheses.

Adaptive hypotheses are centred around the effects and/or benefits of DGC. One such is the hygric hypothesis, focussing on the reduction of respiratory water loss (Buck et al., 1953). Issues of the delivery of oxygen and off-loading of carbon dioxide are addressed in various ways by the oxidative damage, chthonic, respiratory adequacy, and metabolic rate hypotheses (Bradley, 2000; Hetz and Bradley, 2005; Lighton and Berrigan, 1995; Contreras and Bradley, 2009, 2010). The “strolling arthopod” hypothesis proposes that closed spiracles are a mechanism for physical protection from mite infestation (Miller, 1974).

Non-adaptive hypotheses primarily address causes of and/or mechanisms for DGC. The neural hypothesis proposes that DGC occurs as a passive pattern under low brain activity (Matthews and White, 2011a,b, 2013). The emergent property hypothesis poses DGC as a pattern that emerges under certain conditions from the interaction of two feedback loops which directly monitor and regulate endotracheal oxygen (to be sufficient for metabolic demand) and carbon dioxide or haemolymph pH levels (Chown and Holter, 2000; Förster and Hetz, 2010).

It is becoming widely accepted that a combination of these are factors in the presence of DGC, with oxygen and carbon dioxide/ pH regulation as the underlying mechanism, and other aspects providing physiological benefits that may vary across insect types (Contreras et al., 2014; Groenewald et al., 2014).

Förster and Hetz (2010) proposed a theoretical model, in line with the emergent property hypothesis (Chown and Holter, 2000), of a control system composed of two interacting feedback loops. Their data from perfusion experiments indicates that spiracles are open when endotracheal carbon dioxide partial pressure (P_{CO_2}) is above a threshold, or when endotracheal oxygen partial pressure (P_{O_2}) is below a threshold. They therefore described the open and closed spiracle states as steady states in a P_{CO_2}/P_{O_2} phase space (see also Burkett and Schneiderman, 1974), where prolonged time in each of these states would correspond to the open and closed periods of the DGC, and the flutter is viewed as the result of rapid oscillation between the two steady states. The nature of the feedback loops is therefore that they each operate on a simple two-way trigger: when endotracheal P_{O_2} drops low enough, the spiracle is triggered to open, causing a rise in P_{O_2}, raising it back to the threshold value (with a brief lag due to diffusion time), at which point the spiracle closes again. Similarly, when haemolymph pH is low enough—corresponding to simultaneous high endotracheal P_{CO_2}—the spiracle opens, gas exchange lowers the P_{CO_2} level and raises the pH, the trigger value is reached, and the spiracle closes. A key expectation used in this model is that the O_2−related opening and closing triggers would be activated repeatedly in quick succession, giving a flutter effect, while the CO_2−related triggers would be activated on a slower cycle, producing longer open and closed phases. The interaction of these two loops, producing cycles at clearly different frequencies, would therefore produce a DGC-like pattern of open, closed and flutter phases.

In terms of numerical modelling of DGC, early work was done by Snyder et al. (1995), in which the cross-sectional area and volume of the tracheal tube were varied, producing modulation of the DGC phase lengths, thereby highlighting the role of these morphological factors in insect gas exchange patterns.

More recently, in order to investigate the viability of the theoretical model of Förster and Hetz (2010) for interacting systems, Förster undertook computational investigations of each of the two systems independently (Förster, 2010). He simulated the O_2 system, and demonstrated that this feedback loop does indeed produce flutter-like behaviour as expected, and that with multiple, connected tracheal tubes, nonsynchronous spiracle opening and closing is induced by altering the strength of connectivity between the tubes.

To investigate the CO_2 system, Förster performed a bifurcation analysis on the model, and demonstrated through numerical results that oscillations in haemolymph pH occur, as would be caused by the alternation between open and closed spiracle states. His analysis showed particularly that by varying the input parameter values (metabolic rate, buffer values, and spiracular conductance, amongst others), these oscillations would change in amplitude, or disappear altogether, indicating that a steady state had been reached. This investigation shows clearly that a feedback loop with a two-way pH trigger can induce a respiratory pattern of alternating OPs and CPs, if it operates in isolation; and, moreover, that it can induce a steady state (of open or closed spiracles) if there is a variation in critical factors.

Taken together, these two investigations by Förster provide strong support for the idea that DGC is a pattern generated by two interacting feedback loops. However, the critical question about whether such a model can capture realistic DGC patterns (specifically considering relative phase lengths, firstly, but also actual phase lengths) and at the same time remain within physiologically realistic boundaries in terms of, for example, pH and P_{CO_2} ranges, is left unanswered.

We address these issues in a study of the interaction of the two systems, using biologically realistic parameter values based on data from *S. gregaria* and related species (e.g. Groenewald et al., 2012; Harrison et al., 1995; Terblanche et al., 2008). Our primary objective is to establish computationally whether two interacting regulation systems can effectively capture the key DGC behaviour observed, and thereby shed light on whether the underlying mechanism of DGC might indeed be that of two such systems, as simulated.

Furthermore, while such a control systems explanation for DGC seems feasible, the details of such a system should be carefully investigated, and therefore we consider and compare a number of feedback loops, modifications of those described in Förster and Hetz (2010). Such an investigation helps to identify the nature of a system that will generate realistic results, and is useful in giving insight into the relevant physiological processes.

The model is described in detail in Section 2, and results follow in Section 3 before the concluding remarks in Section 4. The final