

Entrainment ranges of forced phase oscillators

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Abstract In the vertebrate spinal cord, a neural circuit called the central pattern generator produces the basic locomotory rhythm. Short and long distance intersegmental connections serve to maintain coordination along the length of the body. As a way of examining the influence of such connections, we consider a model of a chain of coupled phase oscillators in which one oscillator receives a periodic forcing stimulus. For a certain range of forcing frequencies, the chain will match the stimulus frequency, a phenomenon called entrainment. Motivated by recent experiments in lampreys, we derive analytical expressions for the range of forcing frequencies that entrain the chain, and how that range depends on the forcing location. For short intersegmental connections, in which an oscillator is connected only to its nearest neighbors, we describe two ways in which entrainment is lost: internally, in which oscillators within the chain no

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longer oscillate at the same frequency; and externally, in which the the chain no longer has the same frequency as the forcing. By analyzing chains in which every oscillator is connected to every other oscillator (i.e., all-to-all connections), we show that the presence of connections with lengths greater than one do not necessarily change the entrainment ranges based on the nearest-neighbor model. We derive a criterion for the ratio of connection strengths under which the connections of length greater than one do not change the entrainment ranges produced in the nearest-neighbor model, provided entrainment is lost externally. However, when this criterion holds, the range of entrained frequencies is a monotonic function of forcing location, unlike experimental results, in which entrainment ranges are larger near the middle of the chain than at the ends. Numerically, we show that similar non-monotonic entrainment ranges are possible if the ratio criterion does not hold, suggesting that in the lamprey central pattern generator, intersegmental connection strengths are not a simple function of the connection length.

Keywords Entrainment ranges · Coupled oscillators · Locomotion · Central pattern generator

Mathematics Subject Classification (2000) 34C15 · 92B25

1 Introduction

In all vertebrates, the muscle activation patterns for steady locomotory behaviors like swimming and walking are generated by a neural network called the central pattern generator (CPG). This network, located in the spinal cord, can produce the basic rhythm with no sensory input and no descending control from the brain (Cohen and Wallén 1980). Even though the CPG is capable of generating the locomotory rhythm without sensory feedback, it can be strongly modulated by proprioceptive input (i.e., the sense of the body's own movement) (Grillner et al. 1981, 1984; Pearson 1995). In particular, if the CPG oscillates at a frequency ω_0 in the absence of sensory input, a rhythmic stimulus at a frequency ω_f , close to ω_0 , can cause the CPG frequency ω^* to match the stimulus frequency ω_f . We use ω^* to denote the average frequency of the chain during forcing, which may or may not be equal to the forcing frequency ω_f . When the CPG's response is periodic with frequency $\omega^* = \omega_f$ the CPG is said to be *entrained*, and the range of forcing frequencies leading to entrainment is termed the *entrainment range*. Entrainment can be lost in two ways: *externally*, in which all oscillators in the chain have the same average frequency ω^* , but $\omega^* \neq \omega_f$; or *internally*, in which part of the chain has a frequency $\omega = \omega_f$, but the rest of the chain has a different average frequency.

Entrainment of CPGs has been examined experimentally, most notably in lampreys (Williams et al. 1990, Tytell and Cohen 2008, McClellan and Sigvardt 1988), but also in other animals [e.g., leech, Yu and Friesen (2004); locust, Pearson and Ramirez (1990); and cat, Andersson and Grillner (1983)]. The lamprey has also served as a basis for mathematical models (Cohen et al. 1982; Cohen et al. 1992; Ekeberg 1993; Ekeberg and Grillner 1999, Kopell et al. 1991). One fruitful approach, first used by

Cohen et al. (1982), has been to approximate the CPG as a chain of coupled oscillators, in which each oscillator is described by a single variable, its phase θ . Kopell et al. (1988) extended the work in Cohen et al. (1982), deriving general conditions under which a chain of oscillators could maintain synchrony with biologically realistic inter-oscillator phase lags. Later work from Kopell et al. (1991) examined the effect of forcing the chain at one end, and compared their findings to experimental entrainment ranges (Williams et al. 1990). In their mathematical analysis, they considered what they termed “internal entrainment” in which forcing is sufficiently strong that entrainment can only be lost due to changes within the chain of oscillators, such as the forced oscillator assuming a different average frequency from the rest of the chain. Such “clustering” of frequencies has previously been studied by Sakaguchi and Kuramoto (1987), although in that case clustering was caused by random differences in frequencies within the chain, not external forcing.

Despite the focus on internal entrainment in previous mathematical treatments, experimental data from lampreys suggests that entrainment is generally lost externally (E.D.T. and T.K., personal observation). Coupling within the spinal cord is strong (Kiemel et al. 2003), and thus, when the forcing frequency ω_f is far from the baseline ω_0 , oscillators tend to remain synchronized to each other and not to the forcing.

In the current study, we therefore extend previous analytical results by considering both external and internal loss of entrainment. We examine the effect of forcing a chain of phase oscillators not only at either end [like in Kopell et al. (1991)], but also at any location in the middle of the chain, and compare the influence of short- and long-distance intersegmental connections. For short connections, in which each oscillator is connected only to its nearest neighbors, we derive an analytical expression for how the entrainment range depends on forcing location and whether loss of entrainment is internal or external.

We also consider the effect of longer connections on external loss of entrainment. We derive a criterion for the ratio of connection strengths under which longer connections do not change the entrainment ranges produced by nearest-neighbor connections. In this case, the size of the entrainment range is a monotonic function of forcing location. Numerically, we show that non-monotonic entrainment ranges are possible if this ratio criterion of coupling strengths does not hold.

Our modeling results help us to gain insight into recent experimental data from Tytell and Cohen (2008), who extended the experimental protocols developed by Williams et al. (1990) and McClellan and Sigvardt (1988). Briefly, approximately 50 segments of the lamprey spinal cord were dissected out and pinned in a dish containing chilled lamprey saline and an excitatory amino acid, D-glutamate, that activated the CPG circuit. The CPG rhythm was monitored with extracellular records of activity in the ventral root nerves, which contain axons of motor neurons that would activate the muscles in the intact animal. A bending stimulus was applied at points along the spinal cord, and the bending frequency was slowly increased or decreased. The entrainment range was estimated by noting when the CPG maintained a 1:1 synchronization with the bending stimulus [Fig. 1, modified from Tytell and Cohen (2008)].

Tytell and Cohen (2008) found that the entrainment ranges were approximately twice as large for bending stimuli applied near the middle of the preparation than for stimuli at the ends [Fig. 1, modified from Tytell and Cohen (2008)]. They suggested that

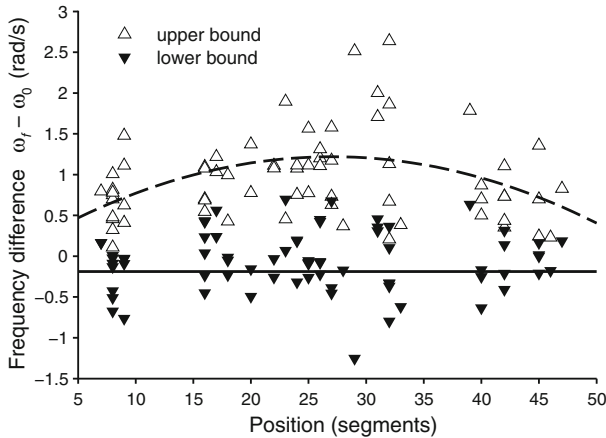


Fig. 1 Entrainment ranges for lamprey spinal cords with sinusoidal bending stimuli at different locations. Open upward-pointing triangles (red online) represent upper entrainment bounds; filled downward-pointing triangles (blue online) represent lower bounds. The dashed and solid lines (red and blue, respectively, online) are the significant terms ($p < 0.05$) from quadratic polynomial fits to the upper and lower bound data, respectively. The quadratic term was not significant for the lower bound regression. Replotted based on data from Tytell and Cohen (2008)

larger entrainment ranges near the middle of the preparation were an intuitive result, because the bending stimulus had to propagate over a shorter distance to entrain the whole chain. In contrast, our results suggest that entrainment ranges that vary non-monotonically as a function of stimulus position are not a trivial result, and, in fact, provide important information about how intersegmental connection strengths vary as a function of length and direction.

2 The model

Below, we first describe the structure of the phase model used to consider entrainment of the lamprey CPG, then consider analytical results for the case when each oscillator is connected only to its nearest neighbor. Next, we extend the nearest-neighbor results, showing that longer connections do not necessarily change the nearest-neighbor entrainment ranges, provided that the strengths of the long connections match a criterion we derive. Finally, we show numerical results for what happens when that criterion does not hold.

To model forcing of the lamprey CPG, we consider a chain of n coupled phase oscillators with the m^{th} oscillator receiving input from a forcing phase oscillator:

$$\dot{\theta}_i = \omega + \sum_{j=1}^n \alpha_{i-j} \sin(\theta_j - \theta_i - \psi_{i-j}), \quad i \neq m \tag{1}$$

$$\dot{\theta}_m = \omega + \sum_{j=1}^n \alpha_{m-j} \sin(\theta_j - \theta_m - \psi_{m-j}) + \alpha_f \sin(\theta_f - \theta_m), \tag{2}$$

$$\dot{\theta}_f = \omega_f, \tag{3}$$

where θ_i for $i = 1, \dots, n$ are the absolute phases (mod 2π) of oscillators in the chain ($i = 1$ for the oscillator nearest the head) and θ_f is the absolute phase (mod 2π) of the forcing oscillator. The parameter ω is the uncoupled angular frequency of the oscillators in the chain, which we assume to be the same for all oscillators. The model assumes that coupling is *translation invariant*, meaning that the properties of the connection from oscillator j to oscillator i only depend on the relative position $k = i - j$: α_k is the strength of the connection and ψ_k is its preferred phase. Here, $k > 0$ for descending (toward the tail, or caudal) connections and $k < 0$ for ascending (toward the head, or rostral) connections. (Note the conflict between the anatomical terms “descending” and “ascending” and our indexing scheme in which i increases from head to tail.) There is no connection between an oscillator and itself, so $\alpha_0 = 0$. Forcing is described by its strength α_f and its angular frequency ω_f .

Unless otherwise stated, we will assume that coupling is *tuned*, meaning that $\psi_k = k\bar{\psi}$, so that the unforced chain has equilibrium relative phases $\theta_j - \theta_i = (i - j)\bar{\psi}$. To model the lamprey CPG, $\bar{\psi}$ should be approximately $2\pi(0.01)$. When coupling is tuned, without loss of generality we can assume that $\bar{\psi} = 0$ by the applying the change of coordinates $\theta_i^{(new)} = \theta_i^{(old)} + i\bar{\psi}$.

To study entrainment, we transform variables from absolute phases to relative phases. Specifically, we use the phase of each oscillator in the chain relative to the forcing oscillator: $\phi_i = \theta_i - \theta_f$, so that the equations of motion become

$$\dot{\phi}_i = \Delta + \sum_{j=1}^n \alpha_{i-j} \sin(\phi_j - \phi_i - \psi_{i-j}), \quad i \neq m \tag{4}$$

$$\dot{\phi}_m = \Delta + \sum_{j=1}^n \alpha_{m-j} \sin(\phi_j - \phi_m - \psi_{m-j}) - \alpha_f \sin \phi_m, \tag{5}$$

where $\Delta = \omega - \omega_f$.

Stable entrainment of the chain corresponds to a stable fixed point of Eqs. (4)–(5) so that the relative phase between each oscillator in the chain and the forcing oscillator is constant in time. [Ermentrout \(1992\)](#) provides sufficient conditions for stable phase-locking of coupled phase oscillators. Suppose that $(\theta_1, \dots, \theta_n, \theta_f)$ are absolute phases for model (1)–(3) such that the relative phases (ϕ_1, \dots, ϕ_n) are a fixed point of (4)–(5). Let A be the following $(n + 1) \times (n + 1)$ matrix whose entries are derivatives of coupling functions:

$$A_{ij} = \begin{cases} \alpha_{i-j} \cos(\theta_j - \theta_i - \psi_{i-j}), & \text{if } i, j \leq n, \\ \alpha_f \cos(\theta_f - \theta_m), & \text{if } i = m \text{ and } j = n + 1, \\ 0 & \text{otherwise.} \end{cases} \tag{6}$$

Ermentrout showed that the relative-phase fixed point is asymptotically stable if $A_{ij} \geq 0$ for all i and j and if every oscillator j *indirectly influences* every other oscillator i , meaning that there are indices i_1, \dots, i_p such that $A_{i,i_1} A_{i_1,i_2} \cdots A_{i_{p-1},i_p} A_{i_p,j} > 0$.

(This corresponds to the matrix being irreducible.) In our case, oscillators in the chain do not indirectly influence the forcing oscillator. However, a straightforward extension of the proof given by Ermentrout shows that stability holds under the weaker assumption that there is one oscillator (the forcing oscillator) that indirectly influences all other oscillators. Therefore, entrainment will be stable if α_f, α_1 and α_{-1} are all positive, $|\theta_f - \theta_m| < \pi/2$, and $|\theta_j - \theta_i - \psi_{i-j}| < \pi/2$ for all i, j such that $\alpha_{i-j} > 0$.

Entrainment ranges for the model were obtained by a combination of analytical and numerical results. Numerically, the limits of the entrainment range were determined by using Newton’s method to find a fixed point of the relative-phase system (4)–(5) with $\phi_m = \pm\pi/2$. These entrainment limits correspond to saddle-node bifurcations of the relative-phase system.

3 Nearest–neighbor coupling

Here we consider the case of tuned nearest–neighbor coupling. As noted above, we can assume that $\psi_k \equiv 0$ without loss of generality. Then, the equations of motion for the relative phases (4), (5) can be written as

$$\begin{aligned} \dot{\phi}_1 &= \Delta + \alpha_{-1} \sin(\phi_2 - \phi_1) - \alpha_{f,1} \sin \phi_1, \\ \dot{\phi}_i &= \Delta + \alpha_1 \sin(\phi_{i-1} - \phi_i) + \alpha_{-1} \sin(\phi_{i+1} - \phi_i) - \alpha_{f,i} \sin \phi_i, \\ &\qquad\qquad\qquad \text{for } i = 2, \dots, n - 1, \\ \dot{\phi}_n &= \Delta + \alpha_1 \sin(\phi_{n-1} - \phi_n) - \alpha_{f,n} \sin \phi_n, \end{aligned} \tag{7}$$

where $\alpha_{f,m} = \alpha_f$ and $\alpha_{f,i} = 0$ if $i \neq m$. For the case of nearest–neighbor coupling, there are only three connection strength parameters α_{-1}, α_1 , and α_f , where α_{-1} is the connection strength from oscillator i to oscillator $i - 1$, an ascending connection, and α_1 represents the strength of a connection from oscillator i to oscillator $i + 1$, a descending connection.

For equilibria to exist, $\dot{\phi}_i = 0$ for all i . In the case $\alpha_1 \neq \alpha_{-1}$, we obtain

$$\begin{aligned} \sin(\phi_i - \phi_{i+1}) &= s_a(i) \stackrel{\text{def}}{=} \frac{(\alpha_1/\alpha_{-1})^i - 1}{\alpha_1 - \alpha_{-1}} \Delta, & \text{for } i < m, \\ \sin(\phi_i - \phi_{i-1}) &= s_d(i) \stackrel{\text{def}}{=} \frac{(\alpha_{-1}/\alpha_1)^{n+1-i} - 1}{\alpha_{-1} - \alpha_1} \Delta, & \text{for } i > m, \\ \sin(\phi_m) &= s_f(m) \stackrel{\text{def}}{=} \frac{\alpha_1(\alpha_1/\alpha_{-1})^{m-1} - \alpha_{-1}(\alpha_{-1}/\alpha_1)^{n-m}}{(\alpha_1 - \alpha_{-1})\alpha_f} \Delta, \end{aligned} \tag{8}$$

which can be verified by direct substitution into the equations of motion. Necessary and sufficient conditions for stable entrainment are that $|s_a(i)| < 1$ for $i < m$, $|s_d(i)| < 1$ for $i > m$, and $|s_f(m)| < 1$. Note that if $i < m - 1$, then

$$\frac{|s_a(i + 1)|}{|s_a(i)|} = \frac{|(\alpha_1/\alpha_{-1})^{i+1} - 1|}{|(\alpha_1/\alpha_{-1})^i - 1|} > 1.$$

Similarly, if $i > m + 1$, then $|s_d(i - 1)|/|s_d(i)| \geq 1$. Therefore, necessary and sufficient conditions for stable entrainment are that $|s_a(m - 1)| < 1$, $|s_d(m + 1)| < 1$, and $|s_f(m)| < 1$. These conditions can be written as

$$|\Delta| < \frac{\alpha_1 - \alpha_{-1}}{(\alpha_1/\alpha_{-1})^{m-1} - 1}, \tag{9}$$

$$|\Delta| < \frac{\alpha_{-1} - \alpha_1}{(\alpha_{-1}/\alpha_1)^{n-m} - 1}, \tag{10}$$

$$|\Delta| < \frac{(\alpha_1 - \alpha_{-1})\alpha_f}{\alpha_1(\alpha_1/\alpha_{-1})^{m-1} - \alpha_{-1}(\alpha_{-1}/\alpha_1)^{n-m}}. \tag{11}$$

If $\alpha_{-1} = \alpha_1 = \alpha$, then the condition obtained by direct substitution into the equations of motion are

$$|\Delta| < \frac{\alpha}{m - 1}, \quad |\Delta| < \frac{\alpha}{n - m}, \quad |\Delta| < \frac{\alpha_f}{n}.$$

As $|\Delta|$ increases, entrainment is lost when any of the three inequalities is violated. Simulations show that immediately after entrainment is lost, the absolute phases $\theta_1, \dots, \theta_n$ and θ_f break into two groups, in which all oscillators in a group have the same average frequency, but the groups have different average frequencies. The nature of the two groups depends on which inequality is violated first. Thus, we can categorize and describe the loss of entrainment as follows:

- **Rostral internal loss of entrainment.** If inequality (9) is violated first, then entrainment is lost when the relative phase between oscillator m and oscillator $m - 1$ (the oscillator immediately rostral to the forcing location) approaches the stability limit $\pm\pi/2$. After entrainment is lost, part of the chain (oscillators m through n) has the same average frequency as the forcing oscillator and part of chain (oscillators 1 through $m - 1$) has a different average frequency.
- **Caudal internal loss of entrainment.** If inequality (10) is violated first, then entrainment is lost when the relative phase between oscillator m and oscillator $m + 1$ (the oscillator immediately caudal to the forcing location) approaches the stability limit $\pm\pi/2$. After entrainment is lost, part of the chain (oscillators 1 through m) has the same average frequency as the forcing oscillator and part of chain (oscillators $m + 1$ through n) has a different average frequency.
- **External loss of entrainment.** If inequality (11) is violated first, then entrainment is lost when the relative phase between oscillator m and the forcing oscillator approaches the stability limit $\pm\pi/2$. After entrainment is lost, the chain of oscillators has a different average frequency than the forcing oscillator.

This last case corresponds to the way that entrainment of the lamprey CPG is thought to be lost as the bending frequency is varied. It is a straightforward exercise to show that the right-hand side of inequality (11) is a monotonic function of the forcing location m , unlike the experimental results in [Tytell and Cohen \(2008\)](#).

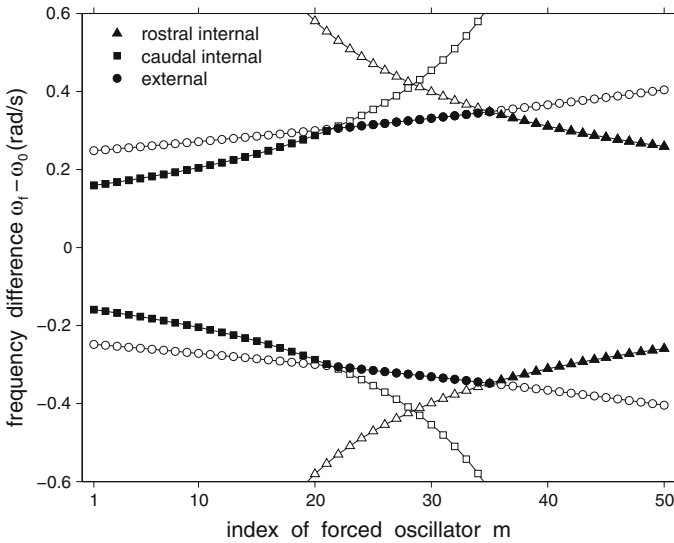


Fig. 2 Entrainment range as a function of forcing location for nearest-neighbor coupling. *Triangles, squares and circles* correspond to constraint Eqs. (9), (10) and (11), respectively, for different types of loss of entrainment. *Closed symbols* show limits of entrainment range. The frequency ω_0 of the unforced chain equals the intrinsic frequency ω of each oscillator

Figure 2 illustrates the three types of loss of entrainment for a chain of 50 oscillators with nearest-neighbor coupling. The connection strengths were chosen to be $\alpha_1 = 10$, $\alpha_{-1} = 10.1$, and $\alpha_f = 16$, so that ascending coupling is slightly stronger than descending coupling. Triangles represent the theoretical limits of the entrainment range for rostral internal loss of entrainment (Eq. 9); squares represent the theoretical limits of the entrainment range for caudal internal loss of entrainment (Eq. 10); and circles represent the theoretical limits of the entrainment range for external loss of entrainment (Eq. 11). For each forcing location $m = 1, \dots, 50$, the entrainment range is smallest of three possible entrainment ranges, as indicated by filled symbols in Fig. 2. For this example, forcing near the beginning of the chain produced caudal internal loss of entrainment, forcing the middle segments of the chain produced external loss of entrainment, and forcing near the end of the chain produced rostral internal loss of entrainment. The largest entrainment ranges are near the middle of the chain. However, this is only true because entrainment is lost internally near either end of the chain. If coupling within the chain were stronger, then entrainment would be lost externally for all locations along the chain, resulting in entrainment ranges whose size increases monotonically from head to tail (the circles in Fig. 2).

Figure 2 cannot be directly compared to experimental data in Fig. 1. Although the two figures look similar, superficially, only the circles in Fig. 2, corresponding to external loss of entrainment, can be compared to the experimental data. The three types of entrainment loss shown in Fig. 2 are only present in a chain with relatively weak coupling, but physiologically, coupling appears to be strong (Kiemel et al. 2003). As

coupling strength increases, the internal entrainment region (bounded by the squares and triangles) becomes larger as a function of α (Eqs. 9 and 10), but the external entrainment region bounded by the circles remains constant (Eq. 11), so that it becomes the only observable entrainment range.

4 All-to-all coupling

Here we consider examples in which all of the oscillators are coupled to all other oscillators, but where coupling strength is a function of connection length and direction. Our consideration of long-distance coupling is motivated by results showing that long connections in the lamprey CPG have substantial coupling strength (Rovainen 1974, 1985; Miller and Sigvardt 2000; Kiemel et al. 2003; McClellan and Hagevik 1999). The equations for an equilibrium of relative phases take the form (4)–(5). Similar to the nearest–neighbor results, we show how the entrainment ranges change as the location of the forcing is moved along the chain.

We first consider a condition under which longer connections do not change the entrainment ranges resulting from the nearest–neighbor connections:

Proposition 1 *If coupling is tuned, and entrainment is lost externally, and*

$$\alpha_k/\alpha_{-k} = (\alpha_1/\alpha_{-1})^k \tag{12}$$

for all lengths $k = 2, \dots, n$, then the entrainment range for forcing at oscillator m is given by equation (11) for nearest–neighbor coupling.

To prove this proposition, from (4) we have that

$$\sin(\phi_i - \phi_m) = \frac{1}{\alpha_{im}} \left(\Delta + \sum_{j \neq m} \alpha_{ij} \sin(\phi_j - \phi_i) \right), \quad \text{for } i \neq m,$$

where we are assuming that $\psi_k \equiv 0$. Substituting this expression into (5) yields

$$\begin{aligned} 0 &= \Delta + \sum_{i \neq m} \frac{\alpha_{m-i}}{\alpha_{i-m}} \left(\Delta + \sum_{j \neq m} \alpha_{i-j} \sin(\phi_j - \phi_i) \right) - \alpha_f \sin \phi_m \\ &= \Delta \left(1 + \sum_{i \neq m} \frac{\alpha_{m-i}}{\alpha_{i-m}} \right) + \sum_{i \neq m} \sum_{\substack{j \neq m \\ j < i}} \left(\frac{\alpha_{m-i}}{\alpha_{i-m}} \alpha_{i-j} - \frac{\alpha_{m-j}}{\alpha_{j-m}} \alpha_{j-i} \right) \sin(\phi_j - \phi_i) \\ &\quad - \alpha_f \sin \phi_m \\ &= \Delta \sum_{k=m-n}^{m-1} \left(\frac{\alpha_1}{\alpha_{-1}} \right)^k - \alpha_f \sin \phi_m, \end{aligned} \tag{13}$$

where we have used that

$$\begin{aligned} \left(\frac{\alpha_{m-i}}{\alpha_{i-m}} \alpha_{i-j} - \frac{\alpha_{m-j}}{\alpha_{j-m}} \alpha_{j-i} \right) &= \alpha_{i-j} \left(\frac{\alpha_{m-i}}{\alpha_{i-m}} - \frac{\alpha_{m-j}}{\alpha_{j-m}} \frac{\alpha_{j-i}}{\alpha_{i-j}} \right) \\ &= \alpha_{i-j} \left(\left(\frac{\alpha_1}{\alpha_{-1}} \right)^{m-i} - \left(\frac{\alpha_1}{\alpha_{-1}} \right)^{m-j} \left(\frac{\alpha_1}{\alpha_{-1}} \right)^{j-i} \right) \\ &= 0. \end{aligned}$$

It is now straightforward to show that solving (13) for $\sin \phi_m$ gives $\sin \phi_m = s_f(m)$ from (8) for nearest-neighbor coupling. Since we are assuming that entrainment is lost externally, Eq. (11) for the entrainment range follows directly from (8).

For example, a choice for the relationship between length and strength is to choose coupling strength to be exponentially decreasing with respect to length, which we term *exponential coupling* (Buchanan and Kasicki 1999; Várkonyi et al. 2008).

In particular, for connections of length k

$$\alpha_k = A_d \exp(-k/\lambda_d), \tag{14}$$

$$\alpha_{-k} = A_a \exp(-k/\lambda_a), \tag{15}$$

where k and $-k$ denote descending and ascending connections, respectively, of length $k = |i - j|$. For exponential coupling,

$$\frac{\alpha_k}{\alpha_{-k}} = \left(\frac{A_d}{A_a} \right)^{k-1} \left(\frac{\alpha_1}{\alpha_{-1}} \right)^k,$$

which implies that the condition (12) in Proposition 1 holds independent of the length constants λ_a, λ_d , provided that $A_a = A_d$.

Figure 3 illustrates an example in which the assumptions of Prop. 1 hold and the entrainment ranges for nearest-neighbor coupling (filled squares) coincide with the entrainment ranges for exponential coupling (open circles). In this example, the parameters for tuned nearest-neighbor coupling are $n = 50, \alpha_1 = 10, \alpha_{-1} = 10.1, \alpha_f = 8, \psi_1 = 2\pi(0.01)$, and $\psi_{-1} = -2\pi(0.01)$, and the parameters for tuned exponential coupling are $n = 50, A_d = A_a = 12, \lambda_d = 1/\log(A_d/10) \approx 5.485, \lambda_a = 1/\log(A_a/10.1) \approx 5.801, \alpha_f = 8$, and $\psi_k = 2\pi k(0.01)$. Figure 3 further illustrates the effects of detuning coupling (changing from tuned to untuned coupling) on the entrainment ranges. If the coupling is detuned by decreasing ψ_k for each descending connection by $2\pi(0.01)$, entrainment ranges change dramatically for nearest-neighbor coupling (filled triangles) but only slightly for exponential coupling (dots). We therefore conclude that the long distance connections cause entrainment ranges to be more robust against model changes such as detuning.

When the conditions of Proposition 1 are met, the size of the entrainment range changes monotonically with forcing location m (closed squares and open circles in Fig. 3). Note that the ratio condition (12) implies that either $\alpha_{-k} \geq \alpha_k$ for all k or $\alpha_{-k} \leq \alpha_k$ for all k , a property that we term *uniform coupling asymmetry*. Based

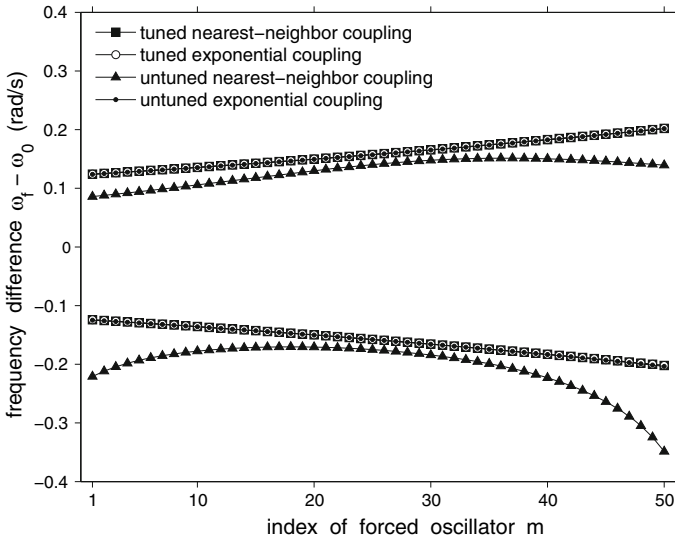


Fig. 3 Nearest-neighbor and all-to-all coupling produce the same entrainment ranges when Proposition 1 holds, but all-to-all coupling is more robust to detuning. For this example, the exponential coupling meets the conditions of Proposition 1 so that tuned nearest-neighbor coupling (filled squares) and tuned exponential coupling (open circles) have the same entrainment ranges (Eq. 11). However, when coupling is detuned by decreasing ψ_k for each descending connection by 2π (0.01), entrainment ranges change dramatically for nearest-neighbor coupling (filled triangles) but only slightly for exponential coupling (dots). For untuned coupling, entrainment ranges were computed numerically. For tuned coupling, the frequency ω_0 of the unforced chain equals the intrinsic frequency ω of each oscillator. For untuned coupling, $\omega_0 \neq \omega$. Note that plotting entrainment ranges in terms of $\omega_f - \omega$ instead of $\omega_f - \omega_0$ would shift ranges by a constant independent of m and, thus, would not affect whether the sizes of the entrainment ranges vary monotonically with m

on numerical results, we offer the following conjecture in which uniform coupling asymmetry is one of a set of sufficient conditions for monotonic entrainment ranges:

Conjecture 1 Assume that coupling is tuned, entrainment is lost externally, and connection strengths decrease monotonically with length: $\alpha_1 \geq \alpha_2 \geq \dots \geq \alpha_{n-1}$ and $\alpha_{-1} \geq \alpha_{-2} \geq \dots \geq \alpha_{-(n-1)}$. If $\alpha_{-k} \geq \alpha_k$ (or $\alpha_{-k} \leq \alpha_k$) for all lengths $k = 1, \dots, n - 1$, then the size of the entrainment range increases (or decreases) monotonically with forcing location m .

Note that the conjecture’s condition of uniform coupling asymmetry is more general than the the ratio condition (12) of Prop. 1, but that the conjecture’s condition of monotonically decreasing connection strengths was not necessary in Prop. 1.

Figure 4a and b illustrates an example of exponential coupling that obeys all the conditions of the conjecture. The ascending connection strength is stronger than the descending connection strength for every length k (Fig. 4a), resulting in an entrainment range whose size increases monotonically with forcing location m (Fig. 4b). Figure 4c and d illustrates an example of exponential coupling that violates the conjecture’s condition of uniform coupling asymmetry; descending connections are stronger for lengths $k \leq 13$ and ascending connections are stronger for lengths $k > 13$ (Fig. 4c).

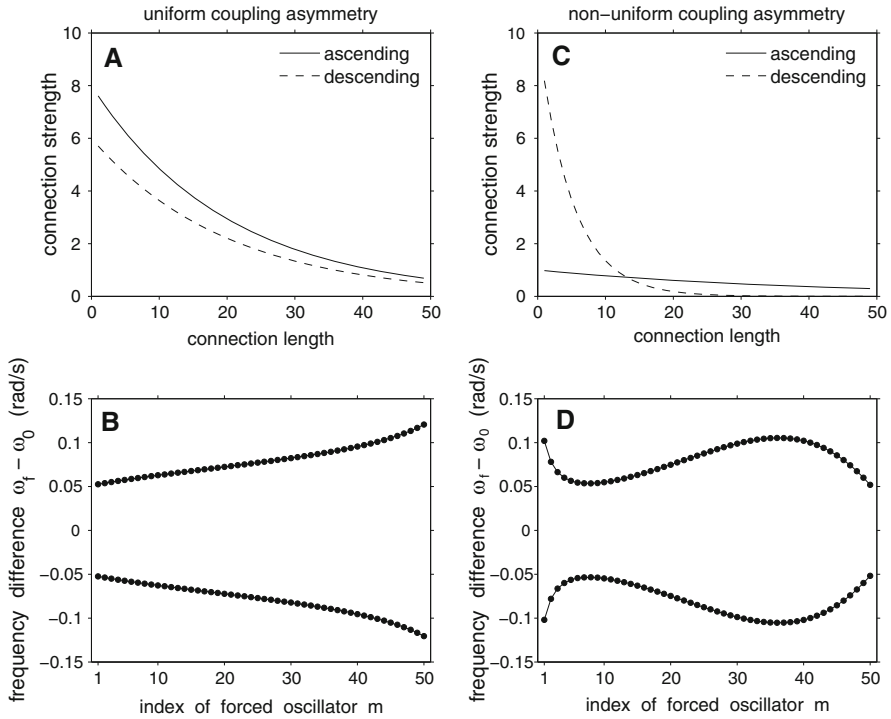


Fig. 4 Entrainment ranges for examples with uniform and non-uniform coupling asymmetry. **a** Connection strengths for an example with uniform coupling asymmetry. Parameter are $n = 50$, $A_a = 8$, $A_d = 6$, $\lambda_a = \lambda_d = 20$, and $\alpha_f = 4$. **b** Resulting entrainment ranges (computed numerically). **c** Connection strengths for an example with non-uniform coupling asymmetry. Parameter are $n = 50$, $A_a = 1$, $A_d = 10$, $\lambda_a = 40$, $\lambda_d = 5$, and $\alpha_f = 4$. **d** Resulting entrainment ranges (computed numerically)

All other conditions of the conjecture hold. The size of the entrainment range is not a monotonic function of forcing position m , but instead shows a peak in the interior of the chain (Fig. 4d), somewhat similar to experimental results of [Tytell and Cohen \(2008\)](#) (Fig. 1). There is also another peak at the head-end of the chain that is not clearly evident in the experimental results, although given the variation in the experimental data its presence cannot be ruled out.

5 Discussion

In this study, we considered a chain of coupled phase oscillators with one oscillator being forced by an external oscillator. By making the specific choice of tuned sinusoidal coupling functions, we were able to completely describe entrainment ranges for nearest-neighbor coupling for forcing at any location along the chain and for any strength of forcing. This description distinguished between internal (within the chain) and external (between the chain and the forcing oscillator) loss of entrainment.

In contrast, the study of [Kopell et al. \(1991\)](#) considered forcing only at either end and assumed that forcing was sufficiently strong so that entrainment could only be lost internally. On the other hand, they considered more general coupling functions than ours. In particular they did not assume that coupling was tuned. This difference is crucial if one considers whether the entrainment range shrinks to zero as the number n of oscillators increases. For tuned coupling, inequality (9) shows that the entrainment range for oscillator n will shrink to zero if $\alpha_1 \geq \alpha_{-1}$ and inequality (10) shows that the entrainment range for oscillator 1 will shrink to zero if $\alpha_{-1} \geq \alpha_1$. Thus, the entrainment range for at least one end of the chain will shrink to zero as n increases. However, [Kopell et al. \(1991\)](#) gives conditions for untuned coupling under which the entrainment range from neither end shrinks to zero.

The preceding indicates that tuned coupling as a simplifying assumption may be misleading if connection lengths are short compared to the length of the chain. This is further illustrated by our results showing that when entrainment is lost externally, the size of the entrainment range for nearest-neighbor coupling is a monotonic function of forcing location for tuned coupling, but not necessarily for untuned coupling (Eq. 11 and Fig. 3). However, our results suggest that the tuned-coupling assumption may be a reasonable approximation when coupling includes substantial long-distance coupling (Fig. 3), as is the case for the lamprey CPG ([Rovainen 1974, 1985](#); [Miller and Sigvardt 2000](#); [Kiemel et al. 2003](#); [McClellan and Hagevik 1999](#); [Ayali et al. 2007](#)).

The results presented here provide an impetus to reexamine experimental data. Specifically, previous entrainment studies, including Tytell and Cohen's study ([Tytell and Cohen 2008](#)), which provided the motivation for this work, along with others ([Williams et al. 1990](#); [McClellan and Sigvardt 1988](#); [McClellan and Jang 1993](#)), did not distinguish between internal and external loss of entrainment. In fact, even though previous theoretical work ([Kopell et al. 1991](#)) only considered internal entrainment loss, the dominant experimental assumption was that entrainment is lost externally ([Tytell and Cohen 2008](#); [Williams et al. 1990](#)). Anecdotal observations indicate that internal entrainment loss, if it is present empirically, is not obvious, particularly when ω_f is not far outside of the entrainment range (E.D.T., T.K., personal observation).

It is possible that larger entrainment ranges observed near the middle of experimental preparations [Fig. 1; [Tytell and Cohen \(2008\)](#)] are due to external entrainment loss, while the smaller ranges near the ends are due to internal loss (as in Fig. 2). The distinction might have been overlooked in experiments due to the method of determining entrainment ranges. Empirically, entrainment is determined by 1:1 synchrony between a sinusoidal bending input and bursts of electrical activity in the motor nerves. If entrainment is lost internally, recordings from nerves close to the forcing would still show 1:1 synchrony, while nerves further away should have an increasing incidence of skipped or doubled bursts. Alternatively, if entrainment is lost externally, the frequency of skipped or doubled bursts will be consistent regardless of the location of the nerve. Looking at average CPG frequency ω^* , as [Tytell and Cohen \(2008\)](#) did, would obscure these subtle differences.

Additionally, our results indicate that internal loss of entrainment is more likely when the forcing strength α_f is strong relative to the internal coupling strengths α_k . In experiments, α_f is thought to correspond roughly to the amplitude of the bending stimulus. Increasing that amplitude would make internal loss of entrainment more likely,

if it is present at all. Specifically, external entrainment loss (Eq. 11) depends on α_f , but internal loss (Eqs. 9 and 10) do not. Increasing α_f thus increases the frequency range at which external entrainment loss occurs, potentially outside of the internal entrainment range (cf. Fig. 2). Similar experiments might also be useful to perform using leech preparations. In leech, entrainment ranges are very large (upper bounds close to twice the baseline frequency ω_0) for forcing near the middle of the chain (Yu and Friesen 2004). As with lampreys, the leech study did not classify the type of entrainment loss, but the large entrainment range indicates relatively strong forcing compared to the internal coupling strength, and the possibility that entrainment might have been lost internally.

In conclusion, our results indicate that non-monotonic entrainment ranges as a function of forcing location, such as observed experimentally in the lamprey CPG, are not a generic property for a chain of coupled oscillators but rather reflect properties of coupling within the chain. Our conjecture suggests that experimental entrainment ranges reflect a non-uniform coupling asymmetry in which ascending connections are stronger for some connection lengths and descending connections are stronger for other lengths. Empirical evidence is divided on the strength and direction of such connections in the lamprey. Kiemel et al. (2003) found a bias toward stronger ascending connections. In contrast, McClellan and Hagevik (1999), using inhibitory baths to examine very long distance connections, found that descending connections were stronger than ascending. Together, these two studies provide some support for our conjecture of non-uniform coupling asymmetry, but further experiments will need to be performed to establish it more thoroughly.

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