

ON PERIPHERAL CONTROL MECHANISMS ACTING ON THE CENTRAL PATTERN GENERATORS FOR SWIMMING IN THE DOGFISH

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SUMMARY

When sinusoidal movements were artificially imposed on the tail region of the curarized spinal dogfish during 'fictive locomotion' the coordinated burst pattern recorded in the ventral roots was effectively entrained to follow movement frequencies above as well as below the resting rate. The entrainment was characterized by: (1) a broad range of effective movement frequencies and amplitudes (down to a few degrees); (2) frequency-dependent timing of entrained bursts to the movement; (3) constant burst durations at low and moderate frequencies; (4) incomplete entrainment in response to high or low movement frequencies combined with a low amplitude; (5) entrainment was still present when mean position of movement was displaced laterally; (6) effects persisted when the tail region was devoid of skin and muscle tissue.

Entrainment effects may be explained by the activation of stretch receptors on either side of the vertebral column–spinal cord, exciting the presumed central pattern generators (CPGs) in the hemisegments ipsilateral to the stretch, while inhibiting the contralateral CPGs.

INTRODUCTION

Coordinated swimming movements are observed in the dogfish after a spinal transection (Steiner, 1886; Bethe, 1899; Le Mare, 1936; Gray & Sand, 1936). Considerable controversy existed for a long time on whether the movements were set up by some sort of reflex chain arrangement (Gray & Sand, 1936; Lissmann, 1946*a, b*; Gray, 1950; Roberts, 1969*a, b*) or were generated by a central network (Le Mare, 1936; cf. von Holst, 1935, 1939). This question was resolved when it was demonstrated that a rhythmic, well-coordinated swim motor pattern could be produced by the spinal cord after the animal had been immobilized by curarization (Grillner, Perret & Zangger, 1976). This was an incontestable demonstration of a central pattern-generating network. However, it was later demonstrated that peripheral input had a strong effect on the central network. Sinusoidal movements imposed on a curarized spinal dogfish could make the efferent ventral root burst activity follow the imposed

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movements (Grillner & Wallén, 1977; cf. also Grillner, McClellan & Perret, 1981). Thus neither the proponents of the central view nor those of the reflex view were entirely wrong, as it has now been shown that a central network interacts with a powerful peripheral input.

Interaction between peripheral input and a central pattern generator has been found for many cases of rhythmic activity, such as respiration (von Euler, 1977), locomotor movements of limbs (Pearson & Duysens, 1976; Grillner & Rossignol, 1978; Andersson *et al.* 1978, 1981; Duysens & Pearson, 1980), wing movements in locusts (Wendler, 1974, 1978) and swimming in tadpoles (Stehouwer & Farel, 1980).

The present study of the dogfish investigates the detailed relationship between the efferent burst activity (such as onset and duration of bursts) and imposed sinusoidal body movements of different amplitude and frequency. The results support the hypothesis that stretch receptors on one side of the vertebral column-spinal cord exert an excitatory effect on the proposed ipsilateral central generators, while inhibiting the contralateral networks, and vice versa.

METHODS

Spiny dogfish (*Squalus acanthias* L.) were anaesthetized with tricaine methane sulphonate (MS-222, Sandoz) in water, and the spinal cord was transected 5–7 segments caudal to the foramen magnum. The general technique was as previously described (Grillner *et al.* 1976; Wallén, 1980).

Preparation and recording of ventral-root activity

The animal was placed in a shallow tank with a continuous flow of sea water through the gills (water temperature 12–18 °C). A dorso-medial incision was made over about 40 segments and muscle tissue trimmed away to expose the vertebral column, which was then rigidly clamped, to eliminate movements, as shown in Fig. 1 A. The tail region caudal to the level of the second dorsal fin was left free so that it could be moved back and forth. Bipolar recordings of the ECG (electrocardiogram) were used to continuously monitor the state of the animal.

The preparation was curarized by injection of D-tubocurarine chloride (3–6 mg/kg) into a caudal, superficial vein (see Wallén, 1980). Ventral roots were dissected free, cut peripherally and recordings were made from them with bipolar silver-ball electrodes connected to preamplifiers (Grass P 15). Signals were distributed to an oscilloscope, a 4-channel ink recorder (Mingograph; straight frequency response up to 750 Hz) and a 4-channel tape-recorder (Tandberg; band width DC – 5 kHz).

Initiation of rhythmic activity

Many preparations exhibited spontaneous bursting activity. In other cases, rhythmic activity was elicited after 5–10 s of tonic stimulation of the rostral end of the spinal cord (0.2–0.8 mA pulses at 50 Hz delivered through 100 μ m copper wires inserted into the spinal cord). The resulting rhythmic activity could then continue spontaneously for minutes or, in some cases even hours. The investigation is based on data from fifteen preparations (length 61–90 cm) which displayed rhythmic activity.

Imposing passive body movements

In the first seven experiments, lateral movements of the tail region were imposed manually by using the tail fin as a 'handle'. The spinal cord was first transected at the base of the fin to eliminate sensory input from the fin. The movable innervated body portion consisted of 19–22 segments (hatched portion of the tail region in Fig. 1A). The region from the rostral border of the movable body portion to the caudalmost ventral root recording (15–21 segments) was firmly fixed by double clamps so that no movements could be transmitted to the recording site.

In the later set of experiments, the tail region (prepared as above) was moved in a more reproducible fashion by means of a stepping motor, controlled by a sine-wave generator. The motor axle was connected to a rigid arm, which was fixed to the denervated part of the tail by sutures. Sinusoidal movements of any desired frequency and amplitude could be imposed in this way. In addition, different lateral positions could be obtained by changing the DC-offset of the sine-wave generator. Both manually imposed movements and motor-driven movements were monitored by a potentiometer connected to the moving part.

In an effort to localize responsible receptors, the innervated tail part in four animals was reduced by removing skin and muscle tissue, ultimately sparing only the vertebral column with its spinal cord.

For comparison, sinusoidal movements of the rostral body portion were imposed in three experiments, by mounting the stepping motor near the head and fixing the arm to the (denervated) snout. The movable, innervated part in this rostral region contained 18–20 spinal-cord segments (hatched portion of the head region in Fig. 1A).

Analysis

All measurements were made manually from ink-writer recordings after rectification and filtering (Paynter filters, time constant 50 ms; Gottlieb & Agarwal, 1970) of the neurograms. Burst amplitudes were measured semiquantitatively as the distance between the base line and a point of 'mean height', half-way between the minimum and maximum levels of the filtered burst discharge. Burst-amplitude values in arbitrary units were thus obtained and have been used merely to illustrate the relative changes in burst amplitude when movement parameters were altered (cf. Fig. 4).

A movement cycle was defined as the interval between the zero transition points where the movement passes the mid-position from right to left (cf. Fig. 3A). The duration of a burst, as well as its time of occurrence in the movement cycle, were normalized by dividing by the movement cycle duration. The resulting phase values could thus range between 0.0 and 1.0 Φ (phase units).

RESULTS

Rhythmical burst discharges can be recorded from the ventral roots in the curarized spinal dogfish (Fig. 1B–D). There is intersegmental coordination as well as strict alternation between the two sides of each segment. This activity corresponds approximately to the neural activity that would normally lead to locomotor movements (Grillner *et al.* 1976). During such 'fictive locomotion', as recorded from the fixed

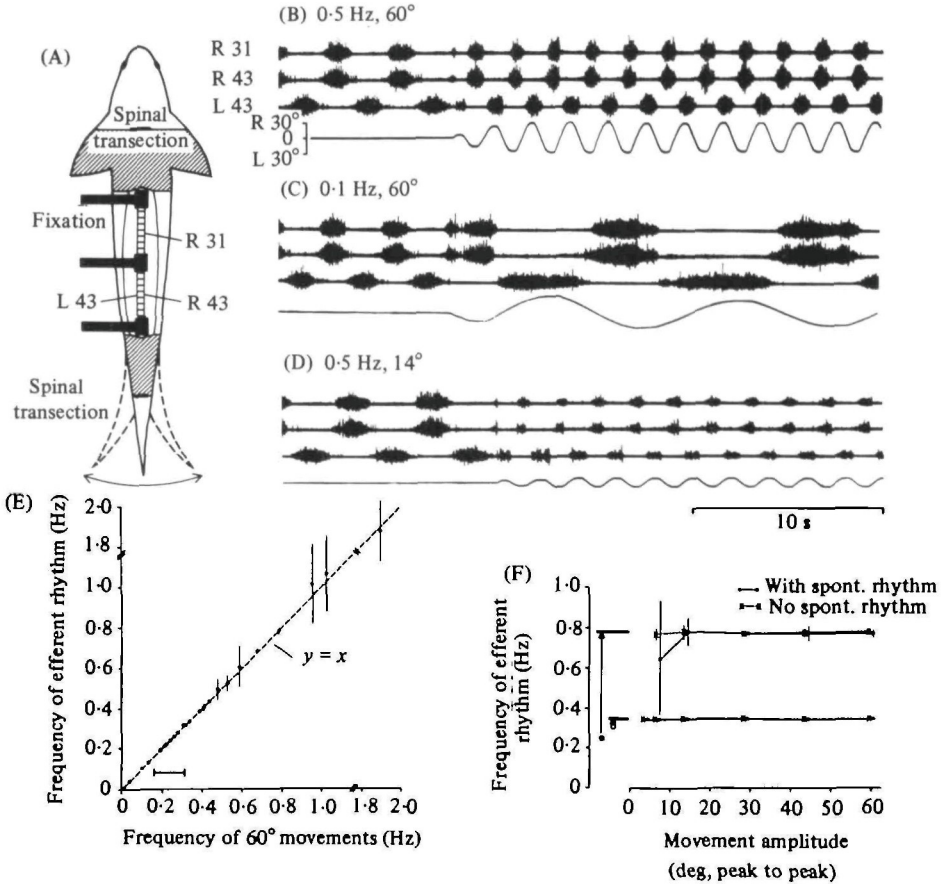


Fig. 1. Entrainment of the 'fictive' locomotor rhythm. (A) Schematic drawing of preparation (see Methods) illustrating the sturdy fixation of the vertebral column and ventral root recording sites (L, left; R, right). Numbering of segments starts with the first segment caudal to the foramen magnum. A lateral movement of the tail region is indicated. (B)–(D) Raw ventral root recordings from segments 31 and 43 in a spontaneously active animal. The tail fin is initially at mid position and is then moved from side to side at different frequencies and peak-to-peak amplitudes as indicated in (B)–(D). Time mark at lower right in (D) applies to all records. (E) The close correlation between frequency of the imposed movement and the entrained rhythm for a broad range of different movement rates (fixed movement amplitude of 60° peak-to-peak). Horizontal bar indicates range of burst rates of the spontaneous rhythm. Each dot represents a mean value (\pm s.d.) of at least ten cycles. (F) The correlation between the efferent rhythm (burst frequency) and imposed movements of either 0.35 or 0.78 Hz frequency (horizontal bars), when movement amplitude (degrees peak-to-peak) was altered. Dots are mean values (\pm s.d.; $n = 10$) when spontaneous bursting was present; crosses (\pm s.d.; $n = 10$) are from sequences without initial spontaneous rhythmicity. Mean burst frequency of the spontaneous rhythms ($n = 10$; s.d. = 0.01 Hz) in each of the two movement sessions are indicated by the open circles. Vertical arrows indicate the discrepancy between the spontaneous rhythm and the imposed movement.

middle part of the animal, the caudal part of the body can be artificially bent from side to side in a way similar to the movements occurring during normal swimming (cf. Fig. 1A). Below is a description of the effect of such applied movements on a variety of parameters in the 'fictive locomotor pattern'.

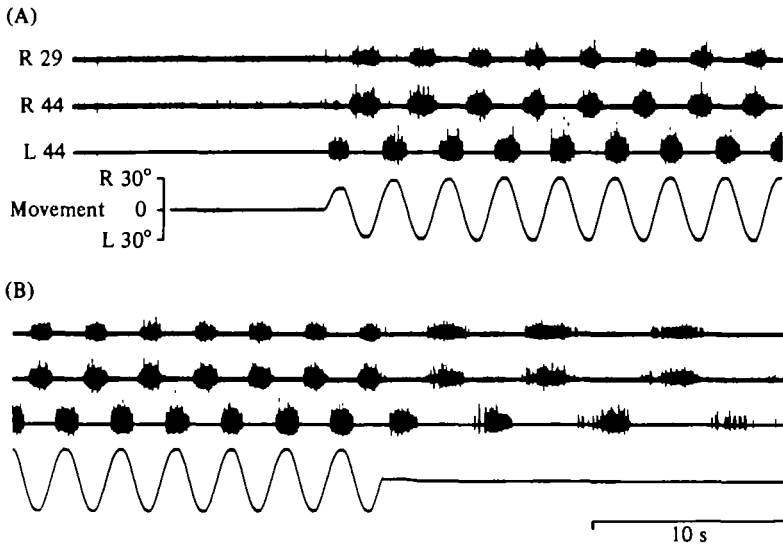


Fig. 2. Sinusoidal movements imposed on the tail region of a preparation with no initial spontaneous rhythmicity. Records show ventral root activity in segments indicated in (A), induced by sinusoidal movements of the tail region of 60° peak-to-peak amplitude at 0.35 Hz (R, right; L, left). The record in (B) is a direct continuation of that in (A).

(1) *Entrainment of the efferent burst rate by sinusoidal passive tail movements of different frequencies and amplitudes*

When the tail was bent from side to side with a sinusoidal time-course the burst activity in all 15 animals tested was modified and became coordinated with the movement cycle (Fig. 1). The efferent bursts were modified directly at the onset of movement (Fig. 1B–D) in both rostral and caudal spinal-cord segments. This applied to movements at a higher (Fig. 1B) as well as a lower rate (Fig. 1C) than the 'resting' burst rate. An effective entrainment with a stable 1:1 relation occurred over a wide range of movement frequencies, as for instance between 0.04 and 1.9 Hz in Fig. 1E. Outside the effective region of 1:1 entrainment the movements still affected the efferent activity in different ways (see below, Section 5).

The burst activity could be entrained by movements of different amplitudes (compare Fig. 1B and D). In Fig. 1F it can be seen that effective entrainment occurs for movements down to 14° peak-to-peak at 0.78 Hz. At 7° in this preparation the bursting followed the movement in a more irregular fashion and not in a fixed 1:1 relation. This is not too surprising since the spontaneous burst frequency was around 0.25 Hz and the imposed movement much faster (see also Section 5). With a slower movement of 0.35 Hz, closer to the spontaneous burst rate (0.31 Hz) entrainment could be obtained down to 4° peak-to-peak (Fig. 1F).

In the absence of initial spontaneous rhythmic efferent activity (see Methods), sinusoidal tail movements in general caused bursting in a strict 1:1 relation to the movement even with small movement amplitudes (Figs. 1F, 2A, 8D, I). Sometimes this burst activity ceased after a few movement cycles (Fig. 8D), but in general it continued throughout the period of imposed movements and for several cycles after the movement was stopped (Fig. 2B). This shows that the network producing the

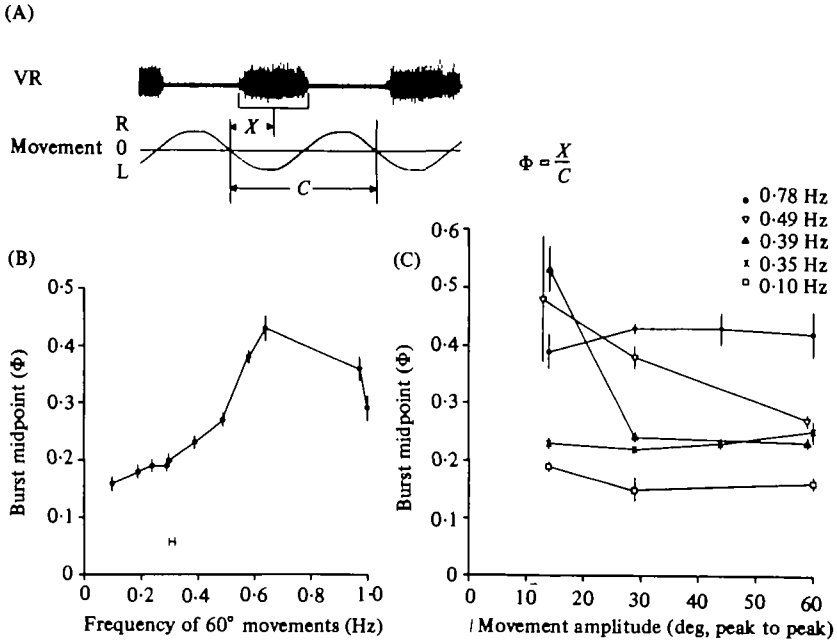


Fig. 3. Phase relation between the movement of the tail region and the entrained rhythm. (A) How measurements of timing between the bursts and the movements were made. The movement cycle duration (C) was measured as described in Methods. The distance between the movement reference point and the midpoint of the burst in the right caudal ventral root (VR) was then measured (X), and the phase value (Φ) of the timing of the burst was calculated as X/C . (B) Dependence of burst timing values (means \pm S.D.; $n = 10$) on the frequency of a 60° movement (peak-to-peak amplitude). The spontaneous burst rate was in this case $0.30\text{--}0.32$ Hz as indicated by the short bar. (C) The relation between burst phase values (means \pm S.D.; $n = 10$) and movement amplitude at five different frequencies as indicated. The 0.35 and 0.78 Hz movements were tested in a preparation with a rest rate of $0.28\text{--}0.35$ Hz. The other three movement frequencies were tested in another preparation, in which rest rate was $0.28\text{--}0.31$ Hz. In both experiments, however, all effects illustrated in (C) were seen.

rhythmic spontaneous activity was activated by the movement. It is thus likely that the efferent bursts were entrained by interaction with this network also in this case. These experiments do not, however, exclude the possibility that there could also be a direct stretch-evoked reflex activation of the motoneurons on both sides (see Discussion).

(2) Timing of burst activity to the sinusoidal movement

In an effort to determine the critical parameters for entrainment, the relationship between imposed movement and timing of burst activity was examined in detail. In Fig. 1 B and C, the burst on one side appears approximately when the body is bent maximally to the contralateral side, but in B the burst clearly comes later in the movement cycle than in C. The occurrence of the burst within the movement cycle can be expressed as the phase value (Φ) of the burst midpoint, calculated as in Fig. 3 A (see Legend). Fig. 3 B shows that the burst appears progressively later in the movement cycle as the frequency of movement was increased. At the highest frequencies the burst was slightly advanced forward again. This change in phase lag was a consistent feature also in other preparations (see Discussion).

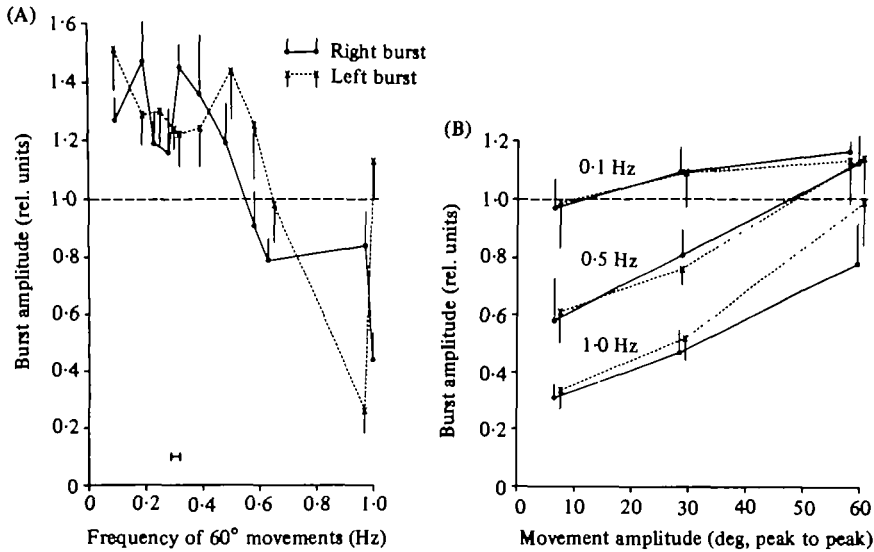


Fig. 4. Effects on the burst amplitude induced by movement of the tail region. Amplitude values are expressed in relative units, obtained by dividing the amplitude value of each burst during an imposed movement with the mean burst amplitude ($n = 8-10$) during the 'resting' activity preceding each movement test. (A) Relative burst amplitudes from the right (dots) and left (crosses) sides of segment 47 (+ or - S.D.s; $n = 9-10$), during 60° movements of different frequencies. Spontaneous burst rate is indicated by the short bar. (B) A plot (symbols as in A) from another preparation of the relation between relative burst amplitudes (segment 43, $n = 8-10$) and movement amplitude at three different frequencies as indicated. Spontaneous burst rate was in this case $0.22-0.30$ Hz.

Fig. 3C shows that the timing of bursts did not depend on movement amplitude (in the range $60-14^\circ$) if movement frequency was near the resting rate ($0.28-0.35$ Hz) or lower, or was much higher (0.8 Hz). However, at intermediary rates (i.e. 0.4 or 0.5 Hz) the bursts come 'early' with large amplitudes. With the smallest amplitudes an entrainment can still be maintained but the bursts slide later in the cycle. The changes in timing of the burst midpoint in the movement cycle are not due to changes of burst duration (see below).

(3) Effects on amplitude and duration of the efferent burst discharge

(A) *Burst amplitude.* Measurements of burst amplitudes (see Methods) were made during imposed sinusoidal movements and compared to the amplitudes during spontaneous, resting rhythmic activity. In Fig. 4 burst amplitudes are expressed as ratios between the amplitude values during the two conditions. A value greater than 1.0 indicates an increase compared to the amplitude during resting activity, whereas a lower value denotes a decreased burst amplitude.

With a 60° movement the amplitude of bursts was enhanced in a frequency range around the resting burst rate ($0.1-0.5$ Hz) and depressed at higher frequencies (Fig. 4A). At around 1 Hz in this preparation, the symmetry between the bursts on the two sides markedly deteriorated.

As movement amplitude was reduced, burst amplitudes decreased to control values at low and intermediate frequencies (0.1 Hz in Fig. 4B). At higher frequencies, a

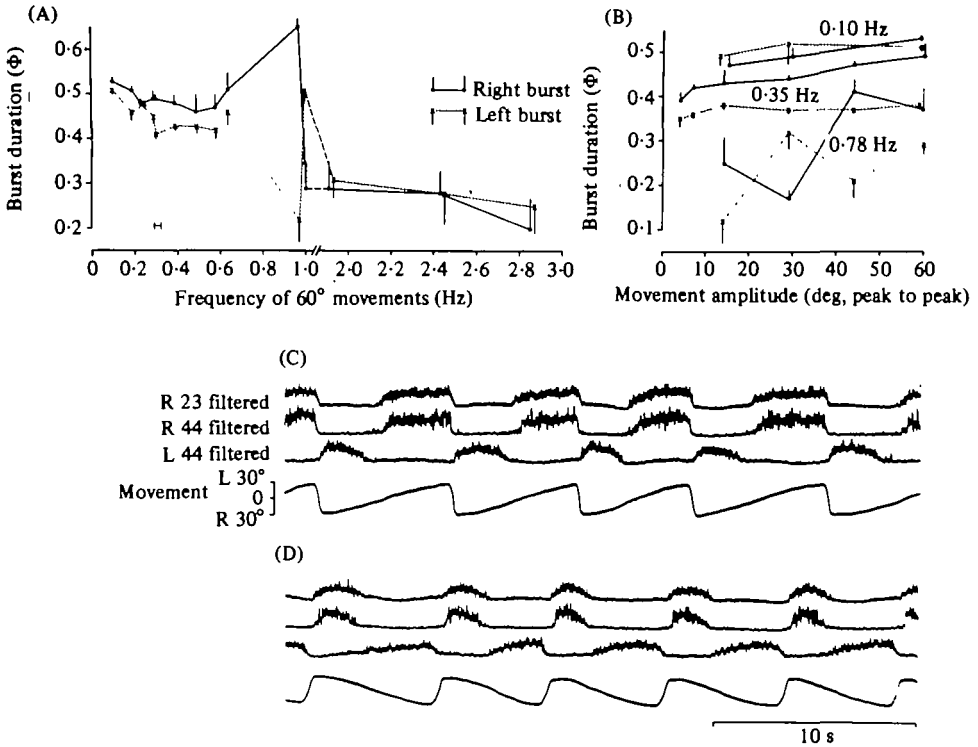


Fig. 5. Burst duration effects elicited by movements of the tail region. (A) The relation between movement frequency and burst duration, expressed as phase values (Φ) of the movement cycle (see Methods). Same preparation as in Fig. 4A. Mean burst durations ($n = 9-10$) on the right (dots; +s.d.s) and left (crosses; -s.d.s) sides of segment 47 have been plotted separately. Note that abscissa has been compressed between 1.0 and 2.0 Hz. (B) A similar plot (symbols as in A) of burst durations versus movement amplitude for three different frequencies as indicated. The 0.1 Hz values are from another experiment (with a rest rate of 0.25-0.29 Hz) than those at 0.35 and 0.78 Hz, where rest rate ranged between 0.28 and 0.35 Hz. The effects illustrated were general in several preparations. In (C) and (D) asymmetric movements of the tail region were imposed manually, so that a slow movement to the left (L, upwards) was followed by a rapid movement to the right (R, downwards; C) or vice versa (D). Ventral root discharges on the right (R) and the left (L) sides of the segments indicated were recorded after rectification and filtering. Time mark in (D) applies to both sets of traces. Spontaneous bursting was symmetrical in this animal.

decreased movement amplitude reduced burst amplitudes even further (0.5 and 1.0 Hz in Fig. 4B). The burst amplitude effects were seen in both rostral and caudal segments.

The above effects were related to movement amplitude and not to movement velocity. For example, 1 Hz movements of 7° and 0.1 Hz movements at 60° have similar mean velocities (approximately 14 and $12^\circ/\text{s}$, respectively), but the corresponding burst amplitudes are markedly different (Fig. 4B). Conversely, a 0.5 Hz movement at 60° (mean velocity about $60^\circ/\text{s}$) gives similar burst amplitude values as the 0.1 Hz movement at 60° .

(B) *Burst duration.* Fig. 5A shows how the normalized duration of the entrained burst (expressed as phase values, i.e. proportion of the movement cycle) varied with

movement frequency. The burst duration phase values during spontaneous rhythmicity (about 0.3 Hz) were rather constant (0.43, s.d. 0.02, and 0.46, s.d. 0.02, for the right and left sides in this preparation). During entrainment, burst duration was slightly prolonged at the lowest frequencies, but otherwise was rather constant up to 0.65 Hz. At 1 Hz, burst durations became different on the two sides (Fig. 5 A, cf. Fig. 4 A). At higher frequencies, the symmetry returned with a reduced burst duration.

Decreasing the movement amplitude from 60° to 4° at a movement rate near rest rate reduced the burst duration by approximately 5% (Fig. 5 B; 0.35 Hz). Even after lowering the movement frequency to 0.10 Hz, the burst duration remained nearly constant for different amplitudes. A higher frequency (0.78 Hz) combined with lower movement amplitudes resulted, however, in a decrease of the burst duration and in addition asymmetry between the two sides.

Asymmetric burst cycles may result from asymmetric movements (Fig. 5 C, D). A rapid movement to the right followed by a slow movement to the extreme left position resulted in a short left side burst and a long burst on the right side (Fig. 5 C). The cessation of right side activity is almost instantaneous with the onset of the movement to the right. With rapid movements to the left, the movement pattern was reversed, as was also the pattern of efferent activity (Fig. 5 D). In addition, the shape of the bursts changed. Long bursts had their peak activity in their later part, whereas short bursts started abruptly with a high level of activity. Note also that in the rostral segment, the right side burst is affected in the same way as its caudal homologue.

Asymmetric burst cycles also resulted when the mean position for sinusoidal movements was displaced towards either side. The mean positions were displaced by 15° from the straight body position, and sinusoidal movements of $\pm 15^\circ$ in amplitude were then imposed. When movements were displaced to the left side, right side bursts were prolonged and left ones shortened (Fig. 6). Displacing the movement to the right side reversed this effect. When movement frequency was altered, asymmetric burst cycles were still produced. For the 0.5 Hz movements, the bursts occur later in the movement cycle (cf. Fig. 3 B). It is noteworthy that burst durations are here changed by shifting both the time of onset and of termination (in opposite directions) so that the burst midpoint remains at about the same phase value.

(4) *Effects on the spontaneous burst pattern induced by changing the position of the tail region*

Since the tail position influences the effects from sinusoidal movements (Fig. 6), it was of interest to test the response to different sustained positions.

If the tail region was bent to progressively more lateral positions, the spontaneous burst pattern changed dramatically (Fig. 7). As the tail was displaced to the left (Fig. 7 A), the activity in the left ventral root ceased, while the burst rate on the right side increased, together with an increasing level of tonic activity. As the tail was moved in the opposite direction the effect was reversed (Fig. 7 B). Here the activity in the rostral right recording disappeared while bursting with reduced amplitude was still maintained in the right caudal segment. When this activity ceased too, the left side became more tonic. It is evident that one side of a segment may burst while no efferent activity occurs in the contralateral ventral root.

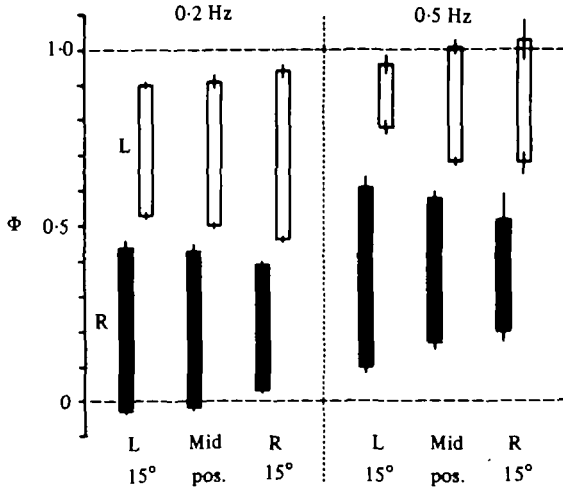


Fig. 6. Asymmetric effects produced by lateral displacements of the mean position of movements of the tail region. Bursts of the entrained rhythm have been plotted as mean phase values (\pm s.d., $n = 10$), in relation to the movement cycle (see Methods). Right side bursts (R; filled bars) as well as left ones (L; unfilled bars) in segment 44 were measured for sinusoidal movements around the mid position (Mid pos.), and for movements whose mean position had been displaced by 15° either to the right (R) or left (L) side. Movements were of 30° peak-to-peak amplitude, thus ranging from the mid position to an extreme position of 30° to the right or left. Movement frequencies were 0.2 and 0.5 Hz.

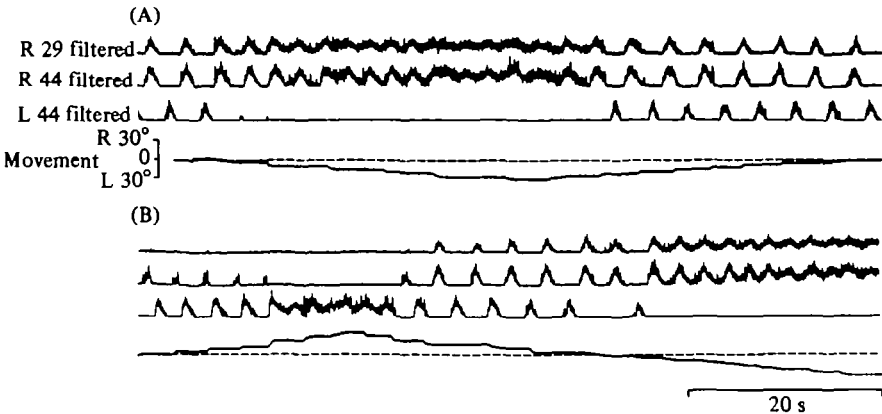


Fig. 7. Effects of displacing the tail region to different lateral positions. Ventral root activity from the segments indicated (R, right; L, left) were recorded after rectification and filtering. The tail region was displaced to progressively more lateral positions to the left side (A), then to the right side and once more to the left side (B). (B) A direct continuation of (A). Interrupted line indicates the mid position. Time mark in (B) applies to both records.

In Fig. 7A it is apparent that the left side stopped bursting as soon as the tail region was displaced past the mid position to the left. However, when the tail was moved back, bursting on the left side resumed well before the mid position was reached. If the tail was kept in a bent position (not shown) for long periods of time (e.g. 1 min or more), the tonic activity on the stretched side would gradually decline and bursting would resume first on this side, and later also on the other side, initially with short bursts giving asymmetric cycles (cf. above, Fig. 6).

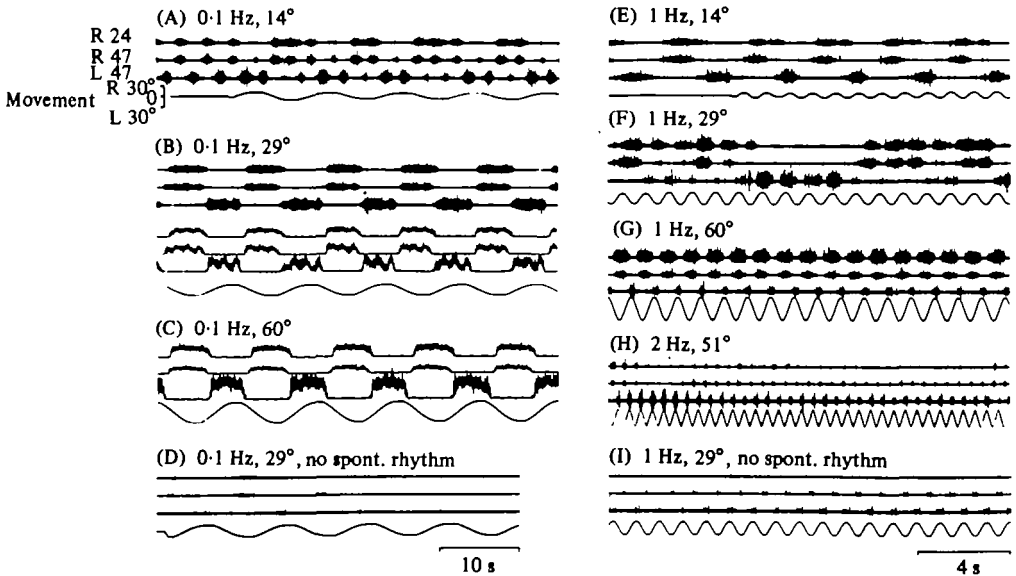


Fig. 8. Incomplete entrainment of the efferent rhythm during movements of the tail region. Ventral root activity was recorded from segments indicated in (A) (applies to all records), and displayed as raw signals except for the ones in (B) (lower traces) and (C), which were rectified and filtered. All movements were sinusoidal and around the mid body position. In (A)–(C), 0.1 Hz movements of different amplitudes (peak-to-peak values as indicated) were imposed when spontaneous activity was present before movement onset (as seen in A). In (D) the same movement as in (B) was imposed, but with no initial spontaneous rhythm. Time mark applies to (A)–(D). In the right hand set of records high-frequency movements were applied. (E)–(G) show the effect of changing the amplitude (peak-to-peak values are indicated) of a 1.0 Hz movement, when spontaneous rhythmicity was present (seen in E). In (I) a movement like that in (F) was imposed when initial spontaneous activity was absent. (H) Entrainment at a movement frequency of 2 Hz. A low level of spontaneous activity (burst frequency about 0.17 Hz) was present before onset of this movement. Time mark in (I) applies to (E)–(I).

(5) Incomplete entrainment of the efferent rhythm

So far only the situation with one burst per movement cycle has been considered. If a high frequency of sinusoidal movement was combined with a low movement amplitude, both burst amplitude and duration may be decreased markedly (Figs. 4, 5). Such a combination of movement parameters may also cause an incomplete entrainment of the burst pattern (Fig. 8E). In addition, incomplete entrainment could occur when an extremely low movement frequency was combined with a low amplitude of movement (Fig. 8A). In this example the spontaneous burst pattern (seen before movement onset) was only slightly modified by the movement. Bursts were modulated in amplitude in accord with the movement cycle. An approximate phase-locking of the rhythm (3–4 bursts per movement cycle) may also be seen with two large bursts (L 47) occurring in approximately the same phase of the movement in each cycle. Increasing the movement amplitude at this frequency (Fig. 8B) resulted in a strict 1:1 phase-locking with the bursts prolonged in proportion to the movement cycle. There is, however, a modulation of the amplitude within each burst (cf. filtered version of records). This activity looks almost like abortive bursts at a frequency

around twice the rest rate (compare to Fig. 8A) and resembles the position effects on the burst pattern shown in Fig. 7. When the movement amplitude was further increased (Fig. 8C) these modulations were no longer apparent.

If a rapid movement of low amplitude (1 Hz, 14°) was imposed (Fig. 8E), the spontaneous rhythm (around 0.3 Hz) was only partly influenced, the bursts were somewhat shortened and their timing modified with a burst phase-locked to every third movement cycle. Also other relations such as 2:1 and 4:1 entrainment could occur. In response to an increased movement amplitude (29° , Fig. 8F) the activity became entrained in a 1:1 relation, but with incomplete activity on either side. Not until the movement amplitude was further increased (60° in Fig. 8G) did the bursting become completely entrained. Movements of 2 Hz were followed in a 1:1 relation (Fig. 8H). However, bursting would periodically cease in one or two of the recorded ventral roots.

(6) *Effects of movements imposed on the rostral body region*

The sinusoidal movements dealt with so far mimic roughly the lateral movements of the tail region during natural swimming. However, all points along most of the body of a swimming fish are displaced laterally, with increasing amplitude towards the tail (Gray, 1933; Grillner & Kashin, 1976). With this preparation, it was possible to investigate the effects of sinusoidal lateral movements applied to the rostral region. The main effect of rostrally imposed movements was a shift in the phase relationship between the movement and the entrained rhythm by about half a cycle (Fig. 9A–D before the bars) as compared to entrainment from the tail region. Deflexion of the head to the left (movement trace upwards) coincides with a burst on the left side whereas deflexion of the tail to the left coincides with a burst on the right side (cf. Fig. 1). Similarly, sustained head displacements to either side (not illustrated) gave rise to tonic activity on the side ipsilateral to the direction of displacement rather than on the stretched side as during tail-region displacements (cf. Fig. 7).

The effects of simultaneously imposed tail part and head movements were also studied. The head region was moved at a fixed rate of 0.3 Hz and with a peak-to-peak amplitude of about 60° by the motor, while the tail region was moved manually. In Fig. 9A–E, addition of tail movements is indicated by the horizontal bars. Moving the tail part at a higher frequency (Fig. 9A), resulted in a change of the burst rhythm so that it now followed the tail movement. A slower movement of the tail region (Fig. 9B) slowed down the rhythm correspondingly. Thus, the influence from the tail movement (also 60° amplitude) was able to override that from the head region.

In Fig. 9C–E the tail was moved with the same frequency as the head region, but with different phase relations. When the tail was moved with a phase difference of 0.5Φ in relation to the rostral movement (i.e. as the head was moved in one direction, the tail was moved in the other), there was no change in timing between the rhythm and the head movement (Fig. 9C). The two timing inputs presumably sum at the same point in the cycle, and no phase-shift occurs. However, a slight tendency for increased burst amplitudes could be seen. When the tail region was moved in phase with the head movement, bursts were shifted relative to the rostral movement cycle (Fig. 9D). Thus, the timing influence from the tail movement again overrode that from the head region. These effects are also illustrated in Fig. 9E, where bursts have

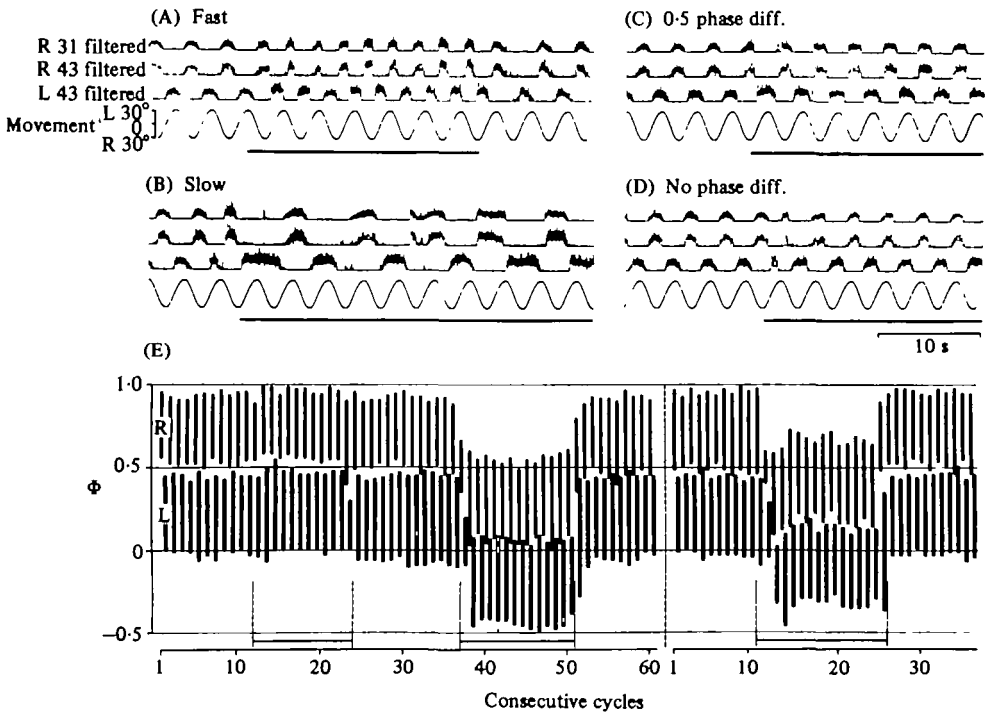


Fig. 9. Sinusoidal movements of the rostral and caudal body regions. (A)–(D) Ventral root activity in segments indicated in (A) (applies for all records) was recorded after rectification and filtering. Movement trace indicates movement of the head (0.3 Hz frequency in all records). Note that an upward deflexion corresponds to a head movement to the left (L), and vice versa. Periods during which a sinusoidal tail movement was simultaneously imposed are indicated by horizontal bars. In all cases both rostrally and caudally imposed movements were of 60° amplitude (peak-to-peak). In (A) the effect of imposing a tail movement of a faster rate than the head movement is illustrated. In (B) the tail movement was slower than that of the rostral region. In (C) and (D) the caudal movement was of the same frequency as the head movement. Phase relation between the two movements was 0.5 Φ in (C) (a movement of the head to, for example, the left coincided with a tail movement to the right and vice versa), whereas in (D) there was no phase difference (a leftward head movement coincided with a leftward movement of the tail region and vice versa). Time scale in (D) is valid for all record traces. (E) A schematic representation of successive cycles that were entrained by head movements of 0.3 Hz frequency and 60° amplitude (peak-to-peak). 0.3 Hz movements of the tail region were simultaneously imposed during cycles indicated by the three horizontal bars. Right (R; filled bars) and left (L; unfilled bars) bursts have been plotted in a normalized fashion (phase), relative to the rostral movement (see Methods). The left horizontal bar corresponds to the sequence shown in (C), while the middle bar corresponds to the sequence in (D). To the right is another movement session where the horizontal bar indicates a tail movement (0.3 Hz) with no phase difference like the one in (D), but with the caudal movement amplitude reduced to 30° (peak-to-peak).

been plotted in phase units of the head movement cycle (see Legend). The left horizontal bar (cycles 12–23) corresponds to the sequence in Fig. 9C, whereas the middle bar (cycles 37–50) indicates the phase-shifted cycles of Fig. 9D. When the tail region was moved with a reduced amplitude (about 30° peak-to-peak) and still in phase with the head movement, the influence from the tail movement was not strong enough to shift the bursts by more than an intermediate value of about 0.3 phase units (Fig. 9E, right horizontal bar).

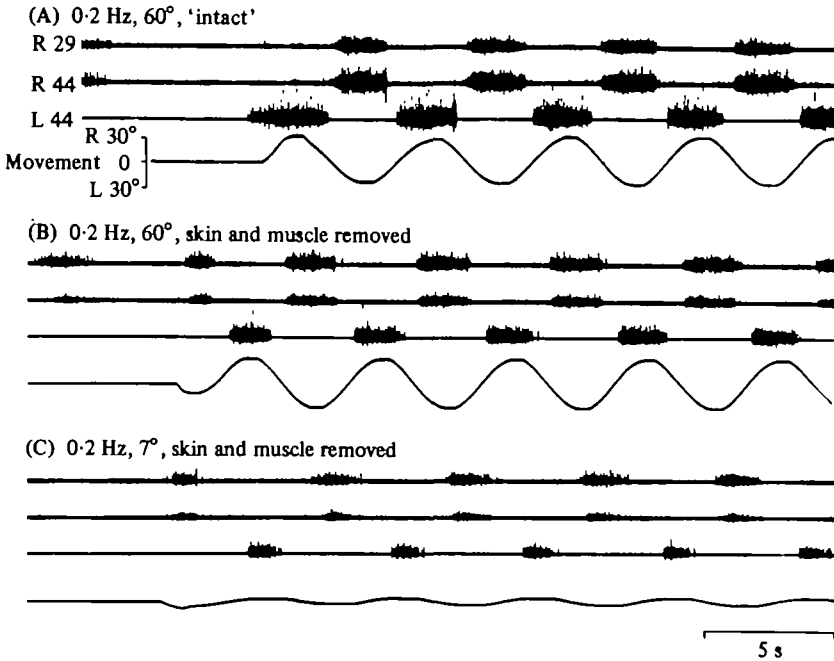


Fig. 10. Entrainment from the tail region after removing skin and muscle tissue. Ventral root activity was recorded from segments indicated in (A), during a 0.2 Hz movement before (A) and after (B, C) skin and muscle tissue had been removed from the tail part (hatched area in Fig. 1A). Movement amplitudes (peak-to-peak) are indicated. A low level of spontaneous activity was present in all situations. In this particular case, amplitudes of entrained bursts in segment 44 appeared somewhat reduced after skin and muscle removal (A, B). Time mark applies to all traces.

(7) Location of receptors responsible for the movement-related feedback

Stretch-sensitive subcutaneous receptors have been described in the trunk region of dogfish (Roberts, 1969*c*). If such receptors were responsible for the entrainment, phasic stretching of the skin could be expected to produce entrainment (without imposing any lateral movement). However, even when large pieces of skin (extending over almost the whole length of the movable, innervated tail part) were stretched rhythmically (not illustrated), no entrainment could be seen. Conversely, when all skin was removed from the tail part, the entrainment persisted during lateral movement of the tail. Subsequently all muscle tissue was trimmed away on the tail part, i.e. the movable part now only consisted of the vertebral column with its spinal cord. A variety of arrangements with clamps were used to assure that the bending effects were not mechanically transmitted to the rostral regions with the skin intact. Nevertheless, a potent entrainment still occurred (Fig. 10) in the four animals which were tested. All effects discussed above remained, including the responses to sustained lateral displacements of the tail part. The effective range of movement frequencies and amplitudes was not significantly diminished in the one experiment where this was studied in more detail. In this case, a 0.2 Hz movement of 7° peak-to-peak was able to entrain the rhythm in a strict 1:1 relation (Fig. 10C). High-frequency movements (2 Hz and 50° amplitude) were also effective. Thus, even though subcutaneous

receptors may contribute, they are not necessary. On the other hand, receptors located in or around the vertebral column–spinal cord have a powerful effect on the pattern generating circuitry.

DISCUSSION

(1) *Normal swimming as compared to the entrained burst pattern*

In several species of fish, during actual swimming as well as after curarization, the duration of the burst activity constitutes an approximately constant fraction of the cycle duration through a large range of burst rates (Grillner, 1974; Grillner *et al.* 1976; Grillner & Kashin, 1976; Williamson & Roberts, 1980; cf. Cohen & Wallén, 1980). In the present study this was also found for the efferent bursts recorded during imposed movements of the tail region through a considerable range of frequencies above and below the rest rate for bursting. In the higher range, however, this burst control partially fails as the bursts become either more variable or much shorter compared to the imposed cycle duration (Fig. 5A). Outside the 1:1 entrainment range the burst activity may return to near rest rate (Fig. 8A) even though a relative (rather than absolute) coordination (von Holst, 1939) may be encountered.

During ordinary swimming, the alternating activity in each segment is phase shifted, with the caudal segments contracting later. A mechanical wave results, which travels down the body with increasing amplitude towards the tail. The neuronal system generates a constant phase lag between each segment (efferent activity) but mechanical factors add to the lag (Grillner, 1974; Grillner & Kashin, 1976). As a rule the EMG activity in one half-segment starts just before this segment has been maximally stretched by the contraction on the contralateral side (intact fish: Grillner & Kashin, 1976; spinal dogfish: Grillner, Rossignol & Wallén, 1977, and unpublished).

The phase relationships between efferent activity and movement are similar in the present experimental situation (Figs. 1, 3) (except at the lowermost frequencies), even though the applied sinusoidal movement only involves the caudal third of the body and furthermore it does not constitute a travelling wave. It is important to note that the phase relationship between efferent bursts and movement is different when the head part is moved instead of the tail. This is presumably related to the fact that the phase lag during swimming between these head and tail segments is approximately half a cycle (Grillner & Kashin, 1976). Due to the anatomical form of the body and the experimental set-up (Fig. 1A), the maximum imposed bending of the tail presumably occurs near the caudal fixation point (i.e. only approximately 20 segments below the caudal recording site). The imposed movement of the compact rostral body portion will probably give maximal bending near the most rostral end of the spinal cord (i.e. approximately 40 segments from the rostral recording site). Thus, local movements at different points along the body clearly can entrain the central network in the entire spinal cord, but the phase relations depend on which region has been moved (Fig. 9). This presupposes an intricate central intersegmental coordination system. It is possible that the afferent signals entrain local spinal cord segments and that central intersegmental mechanisms then cause the remaining spinal cord segments to become active in a coordinated fashion.

During normal swimming in the intact animal the EMG activity tends to start

progressively earlier in the movement cycle with increasing speed, due to the electro-mechanical lags which become more critical as the cycle durations shorten. The increased speed in this case results from an increased central drive. In contrast, in the present experimental situation the central drive is constant and corresponds to the resting rate of the spontaneous burst activity. This allows investigation of the response of the central network to afferent signals at one fixed level of central drive (see also below). The onset of efferent activity when the imposed movement frequency equals that of the spontaneous rest rate is presumably similar to that during normal swimming, but if the imposed movement rate increases, the efferent bursts come progressively later in the cycle until a fixed phase value is reached; at a lower movement rate the bursts appear somewhat earlier in the movement cycle (Fig. 3B). Other preparations in which similar entrainment has been found are usually entrained over a smaller range of movement frequencies (Andersson *et al.* 1981; Grillner *et al.* 1981; Wendler, 1974, 1978). It is therefore surprising that the entrainment with one burst per cycle in this preparation occurs over such a wide range of frequencies (e.g. 0.1–3 Hz with a resting burst rate of 0.3 Hz). Indeed, movement frequencies of 0.1 or 0.05 Hz (cf. Fig. 3E) are too low to be utilized during normal swimming.

It is clear from Fig. 1 and other figures that the central burst pattern immediately becomes entrained by the imposed movement if the frequency and/or amplitude range of the movement is adequate. This demonstrates that the peripheral input caused by the movement acts on the network generating the burst activity under resting conditions. It is noteworthy that movement-induced feedback may in fact stabilize the burst pattern during the application of a brief electrical stimulus to the tail fin; a stimulus which in the absence of movement would severely perturb the rhythm generation (Wallén, 1980).

(II) *Comments on the central pattern generators (CPGs)*

In the dogfish it has been shown that as little as eight segments of the spinal cord can be made to produce burst activity (Grillner, 1974), and in the lamprey four segments may burst (Cohen & Wallén, 1980). The burst-generating network may consist of one CPG unit in each segment or of interconnected circuitry in consecutive segments. In the lamprey spinal cord it is likely that one burst-generating network exists in each hemisegment because both sides of a segment may continue to produce burst activity after a longitudinal midline lesion over several segments (Cohen & Wallén, 1980). In the present experiments (Fig. 7) unilateral bursting was seen when the body was bent to one side or the other. Not only was the activity depressed on one side but the burst activity was accelerated on the active side. The burst cycle duration on the active side depended on whether a burst occurred on the 'silent' side or not. This and other evidence (cf. Wallén, 1980) suggests that also in the dogfish there may be one CPG on each side of the midline, either confined to a single hemisegment or extending over a few neighbouring segments. The networks on the two sides are presumably connected with reciprocal inhibition.

(III) *Does the peripheral input entrain the central pattern generators?*

The supposition made so far is that all movement-induced 1:1 entrainment is caused by a slowing down or speeding up of the central burst generators in the different segments. The situation may, however, be more complicated. For instance, in the case of a slow movement illustrated in Fig. 8B, a 1:1 entrainment occurs, but the activity within each burst is clearly modulated (see Results, section 5). A faster rhythm is present that is not entrained by the movement. If the movement amplitude is increased and thereby the strength of the afferent signal, the entrained bursts appear uniform (Fig. 8C). Conversely, when movement amplitude is lowered (Fig. 8A), 1:1 entrainment is no longer present, but the burst activity is clearly modified during the movement. These data are compatible with the presence of a central rhythm, being modulated by a weak peripheral signal in Fig. 8A, by a dominating afferent input in Fig. 8B (but still with superimposed modulations of central origin), and in Fig. 8C by an even stronger peripheral input causing complete entrainment. When trying to explain these findings, the task may thus be more complex than simply to decide whether or not the CPG network itself is being entrained by the peripheral input.

We may consider three possibilities for the mode of action of the peripheral input. The effects may be exerted (1) on the segmental pattern generator as a functional unit, causing entrainment of its entire activity. Alternatively (2), only a part of the CPG network (i.e. the neurones exciting the ipsilateral motoneurones in each burst) may be directly influenced. A peripheral input could then either 'reflexly' entrain just this part or, indirectly, the whole CPG. A third possibility would be (3) direct action on the motoneurones and not on the CPG. This possibility cannot by itself explain most of the findings, although there is no reason to exclude it as an additional mechanism. For example, the resting CPG activity continues directly over into the entrained activity and vice versa. Furthermore, if (3) would be responsible, the phase relation between movement and burst activity would be expected to remain rather constant and not change with movement rate as was actually observed (Fig. 3A). In addition, the afferent signals would have to block the activity of the CPGs during movements.

Although it is at present not possible to distinguish with certainty between alternatives 1 and 2, there are reasons to favour a mechanism like that of 2. First, the effects shown in Fig. 8(A-C) could be readily interpreted as competing interaction between the directly entrained part and the rest of the CPG network. Secondly, the reduction of burst amplitude and duration seen with movements much faster than rest rate (above 0.6 Hz in Figs. 4A and 5A), may indicate that only part of the network is entrained in this high range. In this case the very large range of apparent (!) entrainment (Fig. 1E) would be misleading, as only a fraction of the range would represent a full 1:1 entrainment of the entire CPG network.

The imposed movement may generate one burst per cycle even when no spontaneous bursting occurs prior to the movement test. After stopping the movement there is as a rule spontaneous bursting for several cycles (Fig. 2B), showing that the CPG network has been affected and thereby contradicting alternative 3 above. Moreover, it is interesting to note that 'entrainment' was easier to obtain in some extreme cases (0.78 Hz, 7° in Fig. 1F) when no initial spontaneous activity was present.

(IV) *Possible mechanism for the entrainment of the CPGs by body movements*(a) *Receptors*

An entrainment may occur after skin and muscle has been removed, which shows that receptors in the vertebral column or spinal cord may elicit the effects (Fig. 10). Stretch-evoked modifications of the efferent rhythmic activity have been observed after a complete dorsal root transection in this preparation (Grillner *et al.* 1976), indicating that ventral root afferents or intraspinal stretch receptors are involved. In the lamprey it has recently been demonstrated that intraspinal stretch sensitive elements exist, and that they may cause an entrainment of the lamprey CPGs (Grillner *et al.* 1981).

(b) *Possible interactive mechanism*

Neural mechanisms for entrainment have been demonstrated in invertebrate pattern generators (Ayers & Selverston, 1979; Pinsker, 1977), largely due to the fact that a detailed knowledge of the generator circuitry was available. Although this is not yet the case in our vertebrate system, we may still ask what type of signals may bring about the entrainment and how they affect the CPGs. The *position* (extreme left or right) has a profound effect on the activity of the CPGs (Fig. 7). The position signal in itself is, however, not sufficient, as very low amplitude sinusoidal movements are effective also when the tail is laterally displaced from the centre position. The phase relationship of the burst midpoint to laterally displaced movements also remains fixed (Fig. 6). At most frequencies (e.g. rest rate) the *movement amplitude* has no effect on the phase relation between burst midpoint and movement (Fig. 3C). Therefore neither velocity nor acceleration can be responsible for the phase-locking, as they both decrease with amplitude when the frequency is kept constant. It rather follows that the timing clues must be the same in all these cases of different amplitudes. We therefore expect the general form of the afferent input volley to be relatively independent of movement amplitude.

Let us consider the simplest possible input signal and interactive mechanism with the CPG that could explain the entrainment. Assuming that the mechanoreceptors have a high static sensitivity and a certain dynamic sensitivity, the afferent input caused by a large-amplitude movement would be expected to have the general form seen in Fig. 11A. A stretch receptor on, for example, the left side will be markedly activated when peak velocity is reached at the midline position. The receptor will then be further activated by the increased degree of stretch until the movement changes direction (peak position), at which point activity will decline. Stretch receptors on the other side of the body will then be activated in the same manner. In the case of a markedly reduced amplitude (interrupted curves in Fig. 11A), the form of the input signal would be scaled down and only slightly modified due to the reduced velocity.

If we assume as suggested above that there is one CPG in each hemisegment, the CPG on the side which is stretched would be facilitated while the contralateral CPG would be depressed (Fig. 11B; cf. Fig. 7 and above). The stretch-evoked facilitation would add to the excitation already present without any movement, i.e. when the CPG is active at rest rate. This stimulus could by itself be sufficient to cause entrain-

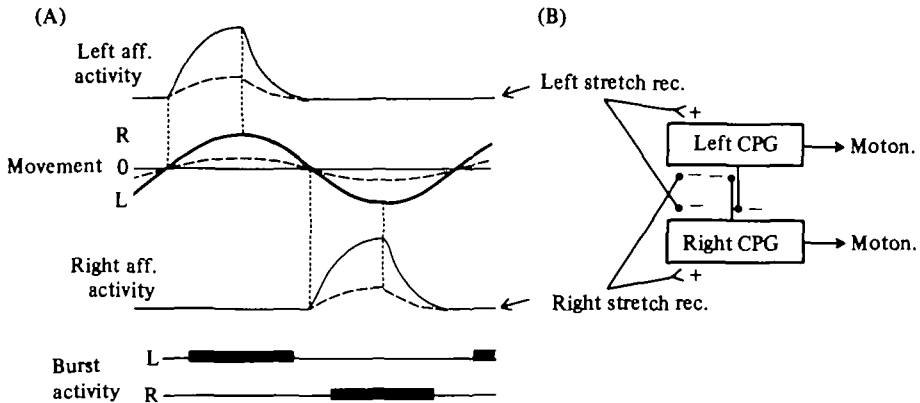


Fig. 11. Tentative scheme explaining the entrainment of the central pattern generators for swimming by stretch receptors. (A) Shows in schematic form the afferent (aff.) activity caused by stretch on the left and right sides. Afferent discharge will start approximately when movement passes the zero transition point (o), and reach its maximum at the extreme position after which activity will drop (dotted lines). A lower movement amplitude will cause a reduced afferent discharge (interrupted curves). Approximate timing of entrained bursts is indicated below (L, left; R, right). (B) Outlines proposed central effects of the afferent signals. Stretch receptors activated when the left side is stretched are assumed to excite (+) the central pattern generator (CPG) in the left hemisegment and inhibit (-) the right CPG and vice versa.

ment. However, in addition the depressing effect on the contralateral CPG would add to the reciprocal effects between the CPGs (Fig. 11 B).

This type of input would assure an effective entrainment by movements of different amplitudes. The size of the stretch-evoked input signals would vary with the amplitude of the movement but the phase values would not change much.

With entrainment frequencies higher than rest rate, the central network is not only made to burst at a higher rate, also the burst duration is decreased in proportion to the movement cycle duration (Fig. 5 A; 0.1–0.6 Hz). This may be a consequence of the network design. Another effect of increasing the frequency is that the bursts appear later (phase) in the movement cycle (Fig. 3 B). It is possible that more 'surplus excitation' is required for the burst to be initiated in this frequency range. This would also explain the delayed initiation of the burst that is seen when decreasing the amplitude of the input signal at intermediary frequencies of entrainment (0.4–0.5 Hz in Fig. 3 C). Furthermore a possible requirement for entrainment is that the burst be initiated before the afferent signal starts to drop, i.e. around peak movement amplitude. This corresponds to the observed maximum in Fig. 3 B.

With entrainment at frequencies lower than rest rate the problem is different. To explain the maintained burst duration (phase) it is in this case not sufficient to rely on the design of the CPG network. The very rapid effect of the movement on the burst activity shows that the burst duration may be controlled instantaneously (e.g. Figs. 1, 5 C, D). The maintained burst activity may therefore result more directly from stretch receptor input, notably from mean position to peak amplitude, i.e. about one-quarter of a cycle (cf. Fig. 11 A). The fact that the burst activity is maintained even longer (i.e. after movement has changed direction; cf. Fig. 1) may be explained if the stretch receptors have a sufficient degree of static sensitivity. While the activity

is maintained on one side, burst initiation is delayed on the other. If this mechanism is sufficient, a directional sensitivity that would act to maintain the burst activity would not have to be invoked as suggested previously (see Grillner, 1979). In this context it is relevant to note that the entrainment at low frequencies breaks down if the amplitude is reduced (cf. Fig. 8A).

If the mean position of the sinusoidal movement is displaced towards either side as in Fig. 6, the afferent input on one side may be strong but on the other weak or absent. In this case there would be a unilateral entrainment, and the contralateral bursts may be made to follow by crossed interactions (Fig. 11B). It would thus be predicted that the phase relations remain constant (midpoint) as found in Fig. 6.

(V) *Functional significance of the feedback control*

Movements are normally initiated by the efferent output rather than by the experimenter. However, it is important to note that the feedback signals are potent enough to modify the duration of an ongoing burst instantaneously (Fig. 1). When the swimming fish goes through one half cycle, the active muscle contraction brings the body from one extreme position to the mid position and soon after that point the antagonist activity is initiated, which will build up the force necessary to stop and reverse the direction of the movement (Grillner & Kashin, 1976). If some external factor slows down or speeds up the movement, the afferent input should prolong or shorten the burst accordingly, so that a proper amount of time is allowed to make the movement proceed to an appropriate amplitude. The reflex input will thus adapt the activity to the varying demands in each cycle. Furthermore the feedback signals will modulate the duration of individual (half) cycles at different levels of central drive from slow cruising to top speed. In fact an intact fish (e.g. trout) maintains a constant amplitude of lateral movements through all except the slowest velocities of swimming (Bainbridge, 1958; Grillner & Kashin, 1976). This type of control would thus optimize the movements in each half cycle, in much the same way as the peripheral input controls the limb in a cat's or cockroach's step-cycle (Pearson & Duysens, 1976; Duysens & Pearson, 1980; Grillner & Rossignol, 1978; Andersson *et al.* 1978, 1981) or presumably during the wing movement of a locust (Wendler, 1974, 1978).

This type of reflex regulation of the output from the CPGs may be of importance under all conditions when the movement cannot be anticipated. In some instances this may be particularly difficult, as when an animal rapidly accelerates. For example, the resistance of the water to the lateral movements of the body will in this case increase markedly. For the propulsion to be as effective as possible the amplitude of the movement should be well regulated. It would seem that an afferent control of this type could be an important factor to optimize the effectiveness of the movements.

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