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Research Article

The Renal Pacemaker System from Unicalyceal Organization to Multicalyceal Coordination

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Abstract

Rhythmic transport in the renal collecting system depends on the initiation, coordination and propagation of smooth-muscle activity. Researchers developed the renal pacemaker concept through complementary anatomical, electrophysiological, and urodynamic investigations in unicalyceal and multicalyceal kidneys. Early morphology identified specialized muscle near the renal attachment of the collecting system. Studies of unicalyceal preparations subsequently distinguished the intrinsic pelvic rhythm from ureteral output and demonstrated regional automaticity consistent with coupled oscillators. Human and porcine studies established multiple calyceal sources, downstream latent automaticity and variable coordination between calyces. Chronic obstruction revealed that preserved local rhythmicity could coexist with impaired transmission and ineffective transport. Grainger and colleagues connected atypical smooth-muscle morphology to identifiable cellular phenotypes and investigated conductances supporting propagation. Yang and colleagues supplied complementary single-cell electrophysiology and multicalyceal functional evidence for HCN-dependent pacemaking. Together, these studies strengthen the cellular basis of the pacemaker concept, although their findings on cell identity and HCN inhibition are not fully reconciled. This review argues that the comparative transition is best understood as an increase in the spatial organization required coordinating distributed oscillators. It is not evidence for a demonstrated linear phylogenetic sequence. The principal unresolved problem is connecting cell-specific rhythm generation to intercalyceal coordination and whole-organ urine transport.

More Information

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Keywords: Renal pelvis; Calyx; Pacemaker; Ureteral peristalsis; Coupled oscillators; Hydronephrosis; Comparative physiology; HCN channels

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Scope and terminology

This is a focused narrative review of selected primary studies, rather than a systematic review or an original experimental report. It considers both the historical development of the pacemaker concept and the comparative organization of the collecting system. Unicalyceal and unipapillate describe related features but are not strictly interchangeable anatomical terms; the same caution applies to multicalyceal and multipapillate. Here, unicalyceal denotes the comparatively simple collecting systems used in the cited rabbit, dog, guinea-pig and mouse experiments, while multicalyceal refers principally to the branching human and porcine systems. Species and preparation are identified when they affect interpretation. For older papers available only through indexed abstracts, discussion is confined to the observations reported there. The review does not claim exhaustive coverage of all subsequent publications.

Introduction

The phrase “renal pacemaker” can refer to three different entities: a rhythm-generating cell, a tissue region initiating a contraction, or the integrated system organizing urine transport. Confusion arises when evidence at one level is treated as proof at another. A rhythmically active strip demonstrates automaticity; an initiating electrical event identifies a potential source; coordinated downstream contraction establishes a further functional relationship. Historical progress depended on separating these observations and then reconnecting them experimentally.

Anatomical studies provided the first strong basis for a specialized proximal control system [1–4]. Functional studies then examined how pelvic rhythms relate to ureteral contraction and urine flow [5–7]. In the multicalyceal kidney, the central question expanded to include how several

calyceal regions contribute to a shared pelvic outlet [8–13]. The cellular investigations of Grainger and Yang extend this progression by testing the identity and conductances of the proposed rhythm-generating apparatus. Their contribution is considered at three distinct levels: cellular phenotype, electrical automaticity and tissue propagation.

"Evolution" requires qualification. The cited experiments compare existing species and preparations; they do not reconstruct ancestral kidneys or establish the direction of anatomical change. Their strongest contribution is a functional account of conserved proximal rhythmicity expressed within different collecting-system architectures. Accordingly, evolution of scientific understanding is distinguished here from inferred biological evolution.

Anatomical foundations of the pacemaker hypothesis

Gosling and Dixon examined human and porcine collecting systems using light and electron microscopy. They identified modified smooth muscle at the renal attachment of minor calyces, continuous with the muscle extending into downstream regions. Its distinctive structure and associated noradrenergic innervation supported the proposal of a proximal pacemaker system [1]. Subsequent porcine ultrastructural work further characterized the specialized calyceal cells [2]. These findings localized a candidate substrate, although cellular appearance did not itself demonstrate spontaneous depolarization or control of neighboring muscle.

The comparative study of Gosling and Dixon explicitly addressed species variation in pacemaker-cell distribution [3]. Later human work described atypical muscle extending between adjacent minor calyces and continuing as an inner layer through the major calyces and renal pelvis, ending around the pelviureteric region [4]. Such continuity offers an anatomical basis for interaction between regions. It does not establish the strength, direction or electrical mechanism of their coupling.

These studies introduced an enduring distinction between specialized rhythm-generating tissue and the more conspicuous contractile musculature. They also made clear why one cannot assume that the collecting system is a uniform muscular conduit. Regional differentiation provides a plausible basis for different intrinsic frequencies and different roles in initiation and propagation.

Unicalyceal physiology and the emergence of distributed control

Constantinou's study of renal pelvic control of ureteral rate was an early physiological milestone [5]. Constantinou and Hrynczuk subsequently measured pelvic activity, ureteral electrical events, and bolus transport in anesthetized dogs. Over the tested flow range, the pelvic pacemaker frequency remained stable, whereas ureteral rate changed in discrete steps. At higher flow, ureteral contractions reached the pelvic rate; additional transport was accommodated through larger boluses [6].

The implication was that the observed ureteral frequency need not equal the intrinsic rhythm of the proximal system. Changes in successful transmission and transported volume can modify output without requiring a proportional acceleration of the source. This distinction established a framework for interpreting flow responses, although its quantitative values are specific to the canine preparation.

The unicalyceal kidney nevertheless cannot be reduced to a single isolated oscillator. Constantinou and Yamaguchi studied whole and dissected rabbit renal pelves and found a proximal-to-distal gradient in spontaneous contraction frequency, without a significant circumferential gradient. A coupled-oscillator simulation reproduced coordinated activity and, under weaker circumferential coupling, modulation of the contraction waveform [7].

The conceptual advance was a hierarchically organized, distributed system within one collecting structure. A dominant output could emerge from interactions among regions with different intrinsic tendencies. The model was a phenomenological explanation of tissue behavior, not a direct measurement of cellular coupling or proof that every regional oscillator was an identical cell type.

Multicalyceal organization and experimental evidence for coordination

Longrigg provided direct human functional support for proximal initiation. Minor-calyx preparations developed regular contractions immediately after isolation, whereas major-calyx and pelvic preparations were initially inactive. Ureteral tissue could become spontaneously active after a delay. Minor-calyx activity was also modifiable by nerve stimulation and adrenergic agents [8]. These observations supported calyceal automaticity with neural modulation and demonstrated that downstream tissue could possess latent rhythmic capacity.

In anesthetized pigs, Constantinou, Silvert and Gosling analyzed ureteral intercontraction intervals at different urine flows. They interpreted the interval distributions as evidence for pacemakers with different fundamental frequencies tending toward synchronism as flow increased [9]. This inference concerned the organization of multiple sources, but was derived from downstream output rather than simultaneous recording of each calyx.

Morita, Ishizuka and Tsuchida then combined direct observation and electrical recording in isolated pig kidneys. Regular activity arose near the borders between major and minor calyces, and waves from upper, middle and lower

regions propagated toward the ureter at different times. Local calyceal pressure corresponded to local electrical events, while pelvic pressure did not directly reproduce calyceal pacemaker activity [10]. This distinction is methodologically important: the pelvis is an integrated output region, and its pressure waveform cannot automatically identify the upstream source.

Hannappel and colleagues studied regional pig strips and proposed primary calyceal oscillators acting with a secondary pacemaker near the pyeloureteral junction [11]. Their model emphasized multiple levels of automaticity. However, spontaneous activity after dissection does not determine leadership in an intact organ, because dissection removes the influence of connected regions.

Calyceal resection supplied stronger intervention-based evidence. Morita and colleagues found that control persisted while at least one major calyx remained intact. Removing all major calyces exposed irregular activity arising from the pelvis, junction and ureteral stump, including retrograde contractions [12]. Thus, calyceal drive helps organize direction and timing; it is not simply one source among equivalent downstream sources. The residual control after partial resection also indicates functional redundancy.

Yamaguchi and Constantinou directly examined intercalyceal timing in 15 arterially perfused pig kidneys. Simultaneous pressure recordings from three calyceal regions and the pelvis demonstrated phase locking, systematic phase oscillation and phase divergence. During phase locking, pelvic contractions were associated with all monitored regions; during phase oscillation, the faster calyceal region was associated with pelvic activity [13]. These observations established that the system has changing coordination states. Similar average frequencies do not necessarily imply synchrony, and a faster region does not invariably dominate independently of coupling.

Comparative interpretation of the two architectures

Table 1 summarizes the comparison. The entries describe the cited experimental systems rather than universal species-independent rules.

The comparative synthesis is therefore a transition from coordination within a relatively simple collecting structure to coordination both within and between calyceal branches. The multicalyceal system adds anatomical convergence: several regions can generate activity, but their effects must be integrated through a shared pelvis. This is a functional interpretation of the combined evidence [7,9–13], not a demonstrated phylogenetic sequence.

The historical sequence also matters. Human and porcine anatomical and functional studies were already contributing to the concept while unicalyceal models were being developed. The field did not proceed in a strictly linear order from rodents to humans. Comparative anatomy, regional recordings and intact-organ urodynamics informed one another.

Hydronephrosis as a disturbance of hierarchy and transmission

Obstructed multicalyceal kidneys revealed that impaired transport need not mean disappearance of the primary rhythm. Mensah-Dwumah, Djurhuus and Constantinou compared isolated pig tissues from normal and chronically obstructed kidneys. Calyceal contraction frequency was similar between groups, whereas pelvic frequency increased toward the calyceal rate [14] (Table 2).

The findings suggest reduced differentiation between regional intrinsic frequencies. They do not demonstrate intact-organ synchrony, nor do they prove selective loss or survival of a molecularly defined pacemaker population. Greater pelvic automaticity could be compatible with competing activity, but that interpretation requires simultaneous regional recording.

The complementary intact-system study by Constantinou and Djurhuus documented bursts, discoordinated contractions and incomplete transmission in chronically obstructed pig kidneys [15]. Djurhuus and Constantinou subsequently described loss of coordination between proximal pelvis, distal pelvis and ureter [16]. Together, these observations support disruption of hierarchical control and propagation. These experiments imposed mechanical obstruction; therefore, the studies mainly show secondary changes in an obstructed system, rather than proving that primary pacemaker disease initiated hydronephrosis.

Table 1: Functional comparison of the collecting-system architectures.

Feature	Unicalyceal evidence	Multicalyceal evidence
Organization	Regional oscillators within one collecting structure [7]	Several calyceal regions converge on a common pelvis [10,13]
Dominant control	Proximal rhythm can organize downstream output [6,7]	Calyceal activity organizes tissues with latent automaticity [11,12]
Flow response	Ureteral rate and bolus size can change without equivalent source acceleration [6]	Output patterns suggest changing synchrony with flow [9]
Coupling evidence	Regional frequency measurements and oscillator simulation [7]	Simultaneous measurements of intercalyceal phase relationships [13]
Key interpretive limit	One calyx does not mean one cellular oscillator	Multiple sources do not imply permanent independence or universal synchrony

Table 2: Spontaneous frequencies in isolated porcine tissue, expressed as contractions/minute, mean ± SD [14]. These are experimental observations, not clinical reference intervals.

Region	Normal	Hydronephrotic
Calyx	9.5 ± 2.2	9.1 ± 2.2
Renal pelvis	4.9 ± 2.1	8.0 ± 4.2

For interpretation, three types of failure should be distinguished: failure to generate activity, failure to coordinate or transmit activity, and failure of a contraction to transport a useful bolus. Classical obstruction studies are especially informative about the second and third. Contraction counts alone cannot distinguish among these possibilities. For functional obstruction and hydronephrosis, the unresolved question is whether defective initiation or propagation among calyces causes clinically significant drainage failure independently of anatomical narrowing. The HCN findings make this plausible, but the studies above do not yet provide a validated patient-level diagnostic test.

For stone disease, the clearest clinical translation currently concerns pressure during treatment. A 2024 randomized trial of 38 patients found that hand-pump irrigation produced higher mean and peak intrarenal pressures than pressurized-bag irrigation, demonstrating that procedural technique materially alters collecting-system mechanics.

Cellular electrophysiology and molecular mechanisms

Cellular work in unicalyceal preparations strengthened the link between morphology and electrical behavior. Klemm, Exintaris and Lang combined recordings and cell identification in guinea-pig tissue. Atypical smooth-muscle cells were concentrated proximally and exhibited pacemaker potentials, whereas typical muscle displayed driven activity [17]. This supplied functional evidence beyond the earlier inference from appearance.

In mouse renal pelvis, Lang and colleagues separately examined electrical signals and intracellular calcium activity in typical muscle, atypical muscle and Cajal-like interstitial cells. Atypical cells exhibited relatively frequent calcium transients and spontaneous transient depolarizations, while typical muscle supported propagated electrical and calcium events [18]. These observations support differentiation between local rhythmic drive and the contractile response. They should not be treated as direct measurements of intercalyceal coordination, which the mouse preparation does not reproduce.

Grainger and colleagues provided a molecular means of identifying the atypical smooth-muscle population [19]. In mouse and cynomolgus-monkey pelvis–kidney junction tissue, PDGFRα was coexpressed with smooth-muscle myosin heavy chain. In mice, genetically encoded calcium indicators demonstrated spontaneous calcium activity in these cells. This connected the historical morphological category to an experimentally identifiable, rhythmically active phenotype. ANO1 expression supplied a candidate depolarizing conductance. Importantly, other PDGFRα-positive cells lacked the smooth-muscle phenotype, and most c-Kit-positive cells were mast cells. Thus, the contribution was a refined cellular classification, not proof that every PDGFRα-positive cell is a pacemaker. Marker expression and calcium activity alone do not demonstrate that an individual cell initiates the organ's rhythm.

Grainger's subsequent mouse study addressed the conversion of proximal activity into propagated contraction [20]. Calcium imaging and contraction measurements supported roles for calcium-activated chloride conductances, likely involving ANO1, and T-type calcium channels in maintaining propagation. Inhibition reduced wave propagation; T-type blockade also reduced contraction frequency. This provides a mechanistic connection to the classical distinction between initiating a rhythm and successfully transmitting it. It does not identify the physical mechanism coupling separate calyces.

An important bridge to multicalyceal anatomy was provided by Hurtado and Smith. They localized HCN3 and $Ca_v3.2$, a T-type calcium-channel isoform, to cells associated with minor-calyx smooth muscle in pigs and humans [21]. This established a candidate molecular signature at the regions implicated by classical anatomy and physiology. Expression remained distinct from evidence that the channels were necessary for rhythm generation.

Yang and colleagues addressed that functional requirement [22]. Immunopurification and patch-clamp recording demonstrated the hyperpolarization-activated inward current, I_h, in isolated mouse HCN-positive cells. Imaging placed these cells within the smooth-muscle network. Human calyceal localization linked the phenotype to multicalyceal anatomy; porcine optical mapping and pharmacological experiments linked HCN blockade to loss of calyceal pacemaker depolarizations and organized peristalsis. These complementary observations support a cellular source capable of electrically driving the musculature. They do not directly establish how multiple calyceal sources synchronize.

The two research programs also expose unresolved differences. Grainger's 2022 mouse experiments found that ZD7288 at 10–30 μM enhanced calcium-wave propagation without suppressing proximal wave frequency [20], whereas Yang's porcine experiments used 100 μM and reported suppression of pacemaker activity [22]. Species, concentration, preparation, and readout differ; these results cannot be presented as equivalent confirmations of HCN dependence. Their reconciliation requires matched experiments and more selective interventions.

Cell identification remains disputed as well. Yang identified sampled PDGFRα-positive, interstitial-like cells as vascular mural cells [22], whereas Grainger identified a PDGFRα-positive, smooth-muscle-myosin-positive population at the pacemaker region [19]. Heterogeneous populations make PDGFRα positivity alone inadequate to resolve this

disagreement. Accordingly, the combined work strengthens the existence of a specialized cellular pacemaker apparatus and conductance-dependent transmission, while leaving its complete molecular classification unsettled.

In the historical narrative, this is a substantive change in explanatory level. Classical regional studies established where activity begins and how its timing relates to downstream events. Cellular identification and perturbation now test which cells and currents can produce that behavior. The resulting synthesis is a specialized rhythm-generating apparatus interacting with excitable contractile tissue, rather than a claim that one marker or channel explains every component of the distributed system.

Evolutionary interpretation and research priorities

The shared proximal organization and cross-species channel findings are consistent with conserved components of renal rhythmic control [1,3,21,22]. A stronger assertion—that a particular ancestral unicalyceal system evolved directly into the human multicalyceal arrangement—would require phylogenetic, developmental and comparative evidence beyond these physiological studies. Anatomical complexity should not be equated with evolutionary rank.

A useful working hypothesis is that local rhythm-generating mechanisms operate within differently arranged networks. The unicalyceal system already requires regional integration; a branching system adds interactions between calyceal units. This hypothesis predicts that preserved local automaticity may coexist with altered global coordination, a prediction compatible with the obstruction experiments [14–16]. It remains a synthesis rather than an established developmental mechanism.

The next experiments should connect source identification, propagation and transport in the same preparation. Simultaneous mapping across multiple calyces, the pelvis, and the ureter should be paired with pressure and bolus measurements during controlled changes in filling. Measurements should include relative phase, initiating region, propagation failures, and transport per contraction, rather than frequency alone. Localized perturbations would help distinguish changes in oscillator frequency from changes in coupling. The Grainger–Yang comparison particularly motivates recordings of membrane voltage, calcium, and contraction in the same tissue, combined with cell-specific channel perturbation and matched drug exposures.

Indeed, studies using porcine kidneys are assumed relatively analogous to human studies, but it remains important to establish whether molecular phenotypes identified in experimental tissue correspond to specific physiological defects. [6,23] Tissue marker changes in diseased specimens cannot independently determine whether a change caused impaired drainage, followed by chronic distension, or reflects differences in sampled cell populations. Linking molecular identity to recorded behavior is therefore more informative than counting stained cells alone.

Conclusion

The renal pacemaker concept has evolved from an anatomical hypothesis of specialized proximal muscle to a functional model of distributed, hierarchically organized rhythmic control. Unicalyceal studies established regional automaticity and distinguished the source rhythm from ureteral output by developing a frequency gradient. Multicalyceal studies demonstrated multiple calyceal sources, dynamic phase relationships, redundancy, and loss of coordination during obstruction. Grainger's work connects the atypical-muscle concept to cellular phenotypes and propagation mechanisms; Yang's work links HCN-positive cells to electrophysiological automaticity and multicalyceal function. These advances support a cellular basis for the pacemaker apparatus without resolving all differences in its molecular identity or ionic dependence. The outstanding task is to explain how cell-level rhythmic activity becomes coordinated urine transport across the branching kidney. Improved identification methods have shown that the calcium-activated chloride channel ANO1 is expressed by pacemaker cells and may contribute to spontaneous depolarization. [23] A better understanding of pacemaker and peristaltic mechanisms is warranted, since aberrant contractile function may underlie diseases such as hydronephrosis, a deleterious condition that can cause significant, irreversible nephron injury.

References

1. Gosling JA, Dixon JS. Structural evidence in support of a urinary tract pacemaker. Br J Urol. 1972;44(5):550–560. Available from: 10.1111/j.1464-410X.1972.tb10122.x.
2. Dixon JS, Gosling JA. The fine structure of pacemaker cells in the pig renal calices. Anat Rec. 1973;175(2):139–153. doi: 10.1002/ar.1091750203.
3. Gosling JA, Dixon JS. Species variation in the location of upper urinary tract pacemaker cells. Invest Urol. 1974;11(5):418–423. Available from: https://pubmed.ncbi.nlm.nih.gov/4856100/
4. Dixon JS, Gosling JA. The musculature of the human renal calices, pelvis and upper ureter. J Anat. 1982;135(Pt 1):129–137. Available from: https://pubmed.ncbi.nlm.nih.gov/7130046/
5. Constantinou CE. Renal pelvic pacemaker control of ureteral peristaltic rate. Am J Physiol. 1974;226(6):1413–1419. Available from: 10.1152/ajplegacy.1974.226.6.1413.
6. Constantinou CE. Upper urinary tract urodynamics: initiation of peristalsis in the upper urinary tract. In: Liao L, Madersbacher H, editors. Handbook of neurourology. Singapore: Springer; 2022. Available from: 10.1007/978-981-16-7939-1_70-1.
7. Constantinou CE, Yamaguchi O. Multiple-coupled pacemaker system in renal pelvis of the unicalyceal kidney. Am J Physiol. 1981;241(5):R412–R418. Available from: 10.1152/ajpregu.1981.241.5.R412.

8. Longrigg N. Minor calyces as primary pacemaker sites for ureteral activity in man. Lancet. 1975;1(7901):253-254. Available from: 10.1016/S0140-6736(75)91145-9.

9. Constantinou CE, Silvert MA, Gosling J. Pacemaker system in the control of ureteral peristaltic rate in the multicalyceal kidney of the pig. Invest Urol. 1977;14(6):440-441. Available from: https://pubmed.ncbi.nlm.nih.gov/870443/

10. Morita T, Ishizuka G, Tsuchida S. Initiation and propagation of stimulus from the renal pelvic pacemaker in pig kidney. Invest Urol. 1981;19(3):157-160. Available from: https://pubmed.ncbi.nlm.nih.gov/7298283/

11. Hannappel J, Golenhofen K, Hohnsbein J, Lutzeyer W. Pacemaker process of ureteral peristalsis in multicalyceal kidneys. Urol Int. 1982;37(4):240-246. Available from: 10.1159/000280826.

12. Morita T, Kondo S, Suzuki T, Ichikawa S, Tsuchida S. Effect of calyceal resection on pelviureteral peristalsis in isolated pig kidney. J Urol. 1986;135(1):151-154. Available from: 10.1016/S0022-5347(17)45551-0.

13. Yamaguchi OA, Constantinou CE. Renal calyceal and pelvic contraction rhythms. Am J Physiol. 1989;257(4 Pt 2):R788-R795. Available from: 10.1152/ajpregu.1989.257.4.R788.

14. Mensah-Dwumah M, Djurhuus JC, Constantinou CE. Hydronephrotic alterations in calyceal and renal pelvic pacemaker function of the in vitro pyeloureteral system. Urol Int. 1980;35(3):161-166. Available from: 10.1159/000280316.

15. Constantinou CE, Djurhuus JC. Pyeloureteral dynamics in the intact and chronically obstructed multicalyceal kidney. Am J Physiol. 1981;241(5):R398-R411. Available from: 10.1152/ajpregu.1981.241.5.R398.

16. Djurhuus JC, Constantinou CE. Chronic ureteric obstruction and its impact on the coordinating mechanisms of peristalsis (pyeloureteric pacemaker system). Urol Res. 1982;10(6):267-270. Available from: 10.1007/BF00255872.

17. Klemm MF, Exintaris B, Lang RJ. Identification of the cells underlying pacemaker activity in the guinea-pig upper urinary tract. J Physiol. 1999;519(Pt 3):867-884. Available from: 10.1111/j.1469-7793.1999.0867n.x.

18. Lang RJ, Hashitani H, Tonta MA, Parkington HC, Suzuki H. Spontaneous electrical and Ca2+ signals in typical and atypical smooth muscle cells and interstitial cell of Cajal-like cells of mouse renal pelvis. J Physiol. 2007;583(Pt 3):1049-1068. Available from: 10.1113/jphysiol.2007.137034.

19. Grainger N, Freeman RS, Shonnard CC, Drumm BT, Koh SD, Ward SM, et al. Identification and classification of interstitial cells in the mouse renal pelvis. J Physiol. 2020;598(15):3283-3307. Available from: 10.1113/JP278888.

20. Shonnard CC, Quiggle SK, Fox EB, Presley H, Daugherty R, Shonnard MC, et al. Propagation of pacemaker activity and peristaltic contractions in the mouse renal pelvis rely on Ca2+–activated Cl- channels and T-type Ca2+ channels. Function (Oxf). 2022;3(6):zqac041. Available from: 10.1093/function/zqac041.

21. Hurtado R, Smith CS. Hyperpolarization-activated cation and T-type calcium ion channel expression in porcine and human renal pacemaker tissues. J Anat. 2016;228(5):812-825. Available from: 10.1111/joa.12444.

22. Yang L, Ricart Arbona RJ, Smith CS, Banks KM, Thomas VK, Palmer L, et al. An evolutionarily conserved pacemaker role for HCN ion channels in smooth muscle. J Physiol. 2023;601(7):1225-1246. Available from: 10.1113/JP283701.

23. Grainger N. Identifying peristaltic pacemaker cells in the upper urinary tract. J Physiol. 2026:3633-3644. Available from: 10.1113/JP284754.