Review

Does the atrioventricular node conduct?

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It is difficult to be certain when the term "conduction" was first applied to the transfer of atrial activation to the ventricles.¹ In 1894, Engelmann used the word "Leitung", which can be translated as "connection" or as "conduction".² In 1906, Tawara described the atrioventricular node, which he termed "Das Reizleitungssystem des Herzens".³ The mechanism of atrioventricular transmission continued to be a subject of considerable debate.⁴⁻⁹ There is a summary of the various mechanisms that were thought to explain atrioventricular transmission in Scherf and Cohen's book on the atrioventricular node.¹⁰ Primarily through the work of Hoffman and Cranefield and their associates,^{11,12} and to a lesser extent others,^{13,14} it became generally accepted that atrial excitation was slowly "conducted" through the atrioventricular node to the His-Purkinje system and the ventricular myocardium.

Hoffman and Cranefield stated that "the excitable cell . . . possesses the same electrical properties as a telegraph cable".¹⁵ Because the "connecting" tissue between the atria and the ventricles was regarded as a series of excitable cells, it followed that the atrioventricular junction was a conduction system. None the less, studies of the complicated structure of the mammalian atrioventricular junction,¹⁴ and the time relation between recorded action potentials from exposed rabbit atrioventricular node^{16,17} have not as yet yielded sufficient data to construct a model of the spatial excitation of the atrioventricular node that is analogous to that of the canine and human ventricles.^{18,19} The atrioventricular node cannot be mapped with the preciseness required to document the sequence of excitation through this part of the specialised conduction system. Although it seems logical to assume conduction through the atrioventricular node, this claim remains open to question and conjecture. Moreover, some observations²⁰ suggest that the traditional concept of the atrioventricular junction as a passive cable with varying electrical properties warrants further examination. The concept of the atrioventricular node as an

oscillator—that is an unprotected pacemaker—may be a somewhat more flexible and biologically sound explanation of the linear and the non-linear functions of the atrioventricular junction.²¹

The concept of the atrioventricular node as an unprotected pacemaker is not new. In 1925, Lewis²² in referring to the work of Mackenzie²³ and Mobitz,²⁴ stated that, "The structure of the A-V node, and its similarity to the S-A node, has suggested the last as the ventricular pacemaker, and it has been thought that a new and distinct wave may start in this after each systole of the auricle".

Functions of the atrioventricular node

A reasonable starting point from which to consider the possibility of the atrioventricular node as an unprotected pacemaker or oscillator is to examine its three functions: (a) synchronisation of atrial and ventricular contraction with appropriate and variable delay depending on the heart rate,²⁵ under conditions of varying autonomic nervous system influences and in different species,^{26,27} (b) protection of the ventricles from excessive atrial rates when there is atrial arrhythmia,^{28,29} and (c) the role as a latent escape pacemaker in the event of atrioventricular block or atrial bradycardia or arrest.³⁰

The atrioventricular node can act as a passive pacemaker and deductive reasoning supports the concept of the atrioventricular node as an electrotonically modulated pacemaker during atrial fibrillation.²⁰ So the question arises as to whether the atrioventricular node, in addition to its pacemaker function, needs to act as a conduit with varying resistive and capacitive properties¹⁵ to perform the three functions or can all functions of the atrioventricular node be explained on the basis of the assumed pacemaker characteristics?

Atrioventricular node as an oscillator (pacemaker)

In 1929 Van der Pol and Van der Mark proposed that the heart beat could be viewed as a relaxation oscillator.³¹ In 1940 Bethe suggested that other

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rhythmic phenomena of the heart, such as a bigeminal rhythm, should also be regarded as oscillatory movements.³² A relaxation oscillator is best described as a condenser that is periodically discharged by the ignition of a neon tube. The frequency of a relaxation oscillator is dependent on the energy supplied and can be increased or decreased by certain external periodic electrical phenomena of small amplitude, such as a sine wave current. In 1973 Van der Tweel *et al* showed that the sinus node of an isolated rat heart could be synchronised the same way as a relaxation oscillator.³³ These observations strongly support the notion that cardiac pacemaker cells may behave, in a physical sense, like relaxation oscillators and, apart from its intrinsic firing rate, the atrioventricular node may not be so different from the sinoatrial node.³⁴ Grant first suggested that the atrioventricular node can be regarded as an oscillator.²¹ Subsequent studies supported this concept.^{35,36} More recently Schamroth *et al* presented evidence that an ectopic pacemaker may be regarded as an oscillator that is synchronised (entrained) by the electrotonic modulation generated by the sinus impulse.³⁷

ATRIAL FIBRILLATION

In 1983 Cohen *et al* developed a quantitative model

for the ventricular response during atrial fibrillation.³⁸ In this model the atrioventricular junction is regarded as the equivalent of a single pacemaker cell characterised by a refractory period and spontaneous phase 4 depolarisation. In 1986 Van der Tweel and co-workers provided experimental evidence that the atrioventricular node may indeed act as a periodically perturbed biological oscillator.³⁹

If we assume that the atrioventricular node acts as an oscillator, can its functions, outlined above, be served and its role in control of cardiac rhythmicity be explained? It is reasonable to assume that the random ventricular rhythm during atrial fibrillation can be the result of electrotonic modulation of phase 4 of the transmembrane action potential^{20,38} of the atrioventricular node by randomly spaced atrial excitations.⁴⁰⁻⁴² Instead of postulating concealed conduction of atrial impulses into the atrioventricular junction⁴³⁻⁴⁵ during atrial fibrillation, let us assume that, depending on the random strength, direction, and timing, the electrotonic effect of the atrial excitation either accelerates diastolic depolarisation of the atrioventricular nodal pacemaker (and thus shortens the RR interval) or decelerates the diastolic depolarisation (hyperpolarise) (and thus lengthens the RR interval) (fig 1). In such a model the ventricular rate and rhythm during atrial fibrillation

Fig 1 Hypothetical model of the atrioventricular nodal pacemaker during atrial fibrillation. Depending on strength, timing, and direction of the atrial impulses, diastolic depolarisation can be speeded up or slowed down (hyperpolarisation) during atrial fibrillation. This explains why the RR intervals vary randomly. This model is an extension of the model of Cohen *et al*.³⁸; RP, refractory period; V_M, voltage of hypothetical monophasic action potential.

Fig 2 Hypothetical model of the atrioventricular nodal pacemaker during sinus rhythm. The ventricular rate and PR interval depend on the sinus rate and the slope of phase 4 depolarisation of the atrioventricular nodal pacemaker. During sinus rhythm or any other organised atrial rhythm the electrotonic effect of the atrial excitations is constant. Varying PR intervals during sinus arrhythmias, long PR intervals of atrial extrasystoles or, for instance, concealed conduction of a non-transmitted P wave can be explained by this model.

would depend on the random electrical properties of the fibrillating atria⁴² and the refractoriness and the intrinsic rate of the atrioventricular nodal pacemaker. The rate of the atrioventricular nodal pacemaker in turn could be increased or decreased by the autonomic nervous system.^{46,47} Similarly, anterograde block during right ventricular pacing in the presence of atrial fibrillation might be attributed to concealed retrograde conduction of the ventricular depolarisations with overdrive suppression of the atrioventricular nodal pacemaker.^{20,48}

Entrainment of the atrioventricular node

If we assume that the atrioventricular node acts as a biological pacemaker or oscillator, then when atrial rhythms are organised atrioventricular "coupling" could result because of synchronisation (entrainment) of the atrioventricular node by the electrotonic spread of the atrial wave of excitation (fig 2).

In 1940 Katz and Schmitt described the electric interaction between two adjacent nerve fibres, which they called "synchronisation".⁴⁹ In 1947 Segers *et al* first referred to possible synchronisation of the atrioventricular nodal pacemaker, namely a fixed temporal relation between the atria and ventricles resulting in isorhythmic dissociation.⁵⁰ This phen-

omenon is known as *acchrochage*, a term which Segers introduced in 1946, when he discovered two fragments of a frog's heart that beat in phase when they were brought into physical contact.⁵¹

DEFINITION OF ENTRAINMENT

Jalife and Michaels defined entrainment as the coupling of a self sustained oscillatory system (such as a pacemaker) to an external forcing oscillation with the result that either both oscillations have the same frequency or the frequencies are related in a harmonic fashion.⁵² Winfree defined entrainment as "The locking of one rhythm to another, with N cycles of the one matching M cycles of the other" and suggested that cardiac pacemaker cells may be synchronised by electrotonic interaction.⁵³ This ability of most non-linear oscillators to entrain or synchronise rests on their time-dependent sensitivity. A probable cellular electrophysiological mechanism responsible for entrainment and synchronisation is an alteration of the rate of phase 4 depolarisation of pacemaker cells. Van der Tweel *et al* in 1973 showed that a pacemaker does not need to be ectopic to be synchronised or entrained.³³ After the introduction of the concept of entrainment in cardiac electrophysiology by Segers *et al*,^{50,51} Moe *et al* sys-

tematically investigated the electrophysiological mechanisms of synchronisation and entrainment of cardiac pacemakers.⁵⁴⁻⁵⁸

Waldo *et al* introduced the term "transient entrainment" to explain the observation that the rate of a tachycardia can be increased by a more rapid electronic pacing rate.⁵⁹ This form of entrainment⁶⁰ differs from the original concept in that the pacemaker rate can not only be increased but also decreased. The concept that we believe to be most appropriate, based on available evidence, is that of the entrained biological oscillator as defined by Winfree^{53, 61} and Jalife and Michaels.⁵²

SINUS RHYTHM

Entrainment of the atrioventricular nodal pacemaker during sinus rhythm by an atrial impulse would explain the paradoxically comparatively short PR intervals in hearts of large mammals such as elephants and whales⁶²⁻⁶⁴ which have much larger atrioventricular nodes than those of human beings.^{65, 66} If during sinus rhythm the atrioventricular node acts as an entrained pacemaker or oscillator, atrioventricular nodal delay need no longer be dependent on the size of the atrioventricular node, or cable length, nor would the short atrioventricular nodal delay in such large hearts conflict with the expected protection against high atrial rates.^{28, 29} This assumption would be strengthened were the atrioventricular nodal pacemaker located at the NH-H border⁶⁷ so that it would promptly activate the His-Purkinje system. The presence of monophasic action potentials with a distinct diastolic depolarisation in the NH-region^{11, 17} localises the atrioventricular nodal pacemaker to that specific area within the atrioventricular node.

The concept of a biological oscillator also explains the shortening of the PR interval during sinus tachycardia induced by sympathetic stimulation or physical exercise. In contrast with atrial tachycardia or rapid atrial pacing (see below), the sympathetic drive not only affects the frequency of the sinus pacemaker and the atrial rate, but also the intrinsic rate of the atrioventricular nodal pacemaker and thus the rate of rise of phase 4 depolarisation. The steeper phase 4, the earlier is the threshold potential reached and the shorter the PR interval (fig 2).

RETROGRADE (VENTRICULOATRIAL) CONDUCTION

In 1959 Scherf used the concept of electrotonic spread to explain retrograde conduction with a relatively short RP interval in the presence of complete atrioventricular block.⁶⁸ Since the strength of the electrotonic spread of the ventricular excitation wave may well exceed that of the atrial excitation

wave it seems logical that retrograde (ventriculoatrial) "conduction" may be present during partial or complete anterograde (atrioventricular) block.^{69, 70} This concept could also explain why structural damage of the atrioventricular junction impairs anterograde conduction more than retrograde conduction. In this setting, however, the geometry of the atrioventricular junction may also be important. If we assume that electrotonic spread can result in retrograde conduction in the presence of atrioventricular block, it is reasonable to expect that it also operates in the absence of atrioventricular block. Similarly, if the electrotonic spread is responsible for retrograde conduction, it may also be the mechanism of anterograde conduction.

Also the findings by Akhtar *et al* that anterograde (atrioventricular) conduction can be affected by retrograde (ventriculoatrial) conduction, and the other way round,⁷¹⁻⁷³ can be explained by electrotonic spread. For instance, a concealed retrogradely conducted ventricular impulse could cause an early resetting of the atrioventricular nodal pacemaker and thus facilitate anterograde conduction.

ATRIAL TACHYCARDIA

If the atrioventricular nodal pacemaker is electrotonically coupled to the sinus node by atrial excitation what is the effect of atrial tachycardias or rapid atrial pacing on atrioventricular nodal function? Atrial arrhythmias with high rates could be blocked by either an insufficiently strong electrotonic effect on phase 4 depolarisation in the presence of a relatively slow intrinsic rate of the atrioventricular nodal pacemaker or by entrainment in a higher harmonic fashion^{35, 52} as, for example, during atrial flutter with atrioventricular block. Van der Tweel *et al* have shown that this manifestation of entrainment operates at the level of the sinoatrial node of isolated rat hearts.³³ There is probably an upper limit to which the intrinsic oscillatory rate of the atrioventricular nodal pacemaker can be increased by an artificial pacemaker or an ectopic focus. At that point its rate can no longer be enhanced through entrainment by the artificial atrial pacemaker. Long PR intervals, and, subsequently, Wenckebach periodicity may result when the atrial and the atrioventricular nodal pacemaker rates are out of phase. Wenckebach type I atrioventricular block may also result from damage below the assumed location of the atrioventricular nodal pacemaker, from too low an intrinsic rate of the atrioventricular nodal pacemaker, or from impaired conduction in the His-Purkinje system. In the absence of sympathetic influences the rate of phase 4 depolarisation does not increase and it takes longer to reach threshold. The coupling of the ventricles to the atria occurs at the

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moment the electrotonic spread of the atrial excitation reaches the atrioventricular nodal pacemaker. An impulse arriving early in diastole or in the presence of a slow phase 4 depolarisation, or both, will result in a long PR interval. On the contrary, an impulse arriving late in diastole or in the presence of a fast phase 4 depolarisation, or both, will result in a short PR interval (fig 2).

ACCESSORY PATHWAYS

In the presence of a Kent bundle or other accessory pathways the concept of the atrioventricular node as an oscillator would change the current notion that competition between two conduction pathways with different electrophysiological properties is the mechanism of Wolff-Parkinson-White syndrome.⁷⁴⁻⁷⁶ The competition (fusion) would rather be between a passive, at times rapidly conducting pathway and a synchronised, entrained biological oscillator located in the atrioventricular node. Conduction through the accessory pathway that results in ventricular excitation could either cause override suppression of the atrioventricular node and thus force the atrial impulse to proceed along the accessory pathway, or it could reset the atrioventricular nodal pacemaker and activate the atrial myocardium, resulting in an atrioventricular reentrant tachycardia.

Conclusion

There can be no doubt about the importance of electrotonus as the mechanism of otherwise inexplicable arrhythmias.⁷⁷⁻⁸⁰ In this presentation the atrioventricular node is regarded as a biological oscillator and electrotonus induced by organised atrial or ventricular excitation as the mechanism by which the oscillator can be entrained.

The concept of the atrioventricular node as an oscillator/pacemaker influenced by electrotonus is in keeping with the functions of the atrioventricular node and offers a rational explanation for the varying atrioventricular nodal delay during sinus rhythm, the protection the atrioventricular node affords in the presence of atrial tachycardias and fibrillation, and for atrioventricular nodal automaticity as an escape mechanism. The concept accords with clinical and experimental observations that classically have been attributed to the "conducting" properties of the atrioventricular junction. It also offers a rational explanation for the relatively short PR intervals in large mammals such as elephants and whales, as well as for several atrioventricular "conduction" abnormalities and arrhythmias. In fact, the assumption that conduction and automaticity are properties of the atrioventricular node tends to complicate rather than to clarify the understanding of atrioventricular

nodal function under varying physiological and pathological influences.

The question whether the atrioventricular node conducts in the traditional meaning of the word warrants further investigation.

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References

- 1 Fye WB. The origin of the heart beat: a tale of frogs, jellyfish, and turtles. *Circulation* 1987;76:493-500.
- 2 Engelmann TW. Beobachtungen und Versuche am suspendierten Herzens. *Pflügers Archiv f d ges Physiol* 1894;56:149-202.
- 3 Tawara S. *Das Reizleitungssystem des Herzens*. Jena: Fischer, 1906.
- 4 Aschoff L. Referat über die Herzstörungen in ihren Beziehungen zu den spezifischen Muskelsystemen des Herzens. *Verh d path Ges* 1910;14:3-35.
- 5 Von Hösslin H. Über Veränderungen der Kammerkomplexe im Elektrokardiogramm bei normaler Vorhofstätigkeit und Vorhofflimmern. *Zeitschr f d ges exp Med* 1923;34:358-72.
- 6 Mobitz W. Über die unvollständige Störung der Erregungsüberleitung zwischen Vorhof und Kammer des menschlichen Herzens. *Zeitschr f d ges exp Med* 1924;4:180-237.
- 7 Donzelot E. La dualité normale de l'automatisme cardiaque. *Arch Mal Coeur* 1924;17:409-14.
- 8 Vaquez H, Donzelot E. Physiologie du rythme cardiaque. *Arch Mal Coeur* 1925;18:353-70.
- 9 Gilson AS Jr. The locus and the nature of the A-V pause in the spread of cardiac activation. *Am J Physiol* 1942;138:113-25.
- 10 Scherf D, Cohen J. *The atrioventricular node and selected cardiac arrhythmias*. New York: Grune and Stratton, 1964:23-32.
- 11 Hoffman BF, Paes de Carvalho A, de Mello WC. Transmembrane potentials of single fibres of the atrioventricular node. *Nature* 1958;181:66-7.
- 12 Hoffman BF, Cranefield PF. Microelectrode studies of possible mechanisms of atrioventricular delay. *Physiologist* 1959;2:59-60.
- 13 Scherf AM, Rodriguez MI, Liikane J, Young AC. The mechanism of atrioventricular conduction. *Circ Res* 1959;7:54-61.
- 14 Van der Kooi MW, Durrer D, Van Dam RTh, Van der Tweel LH. Electrical activity in sinus node and atrioventricular node. *Am Heart J* 1956;51:684-700.
- 15 Hoffman BF, Cranefield PF. *Electrophysiology of the heart*. New York: McGraw-Hill, 1960:23 ff.
- 16 Janse MJ. Influence of the direction of the atrial wave front on A-V nodal transmission in isolated hearts of rabbits. *Circ Res* 1969;25:439-49.
- 17 Mazgalev T, Dreifus LS, Iinuma H, Michelson EL.

- Effects of the site and timing of atrioventricular nodal input on atrioventricular conduction in the isolated perfused rabbit heart. *Circulation* 1984;70:748-59.
- 18 Durrer D, Van der Tweel LH. Excitation of the left ventricular wall of the dog and goat. *Ann NY Acad Sci* 1957;65:779-803.
 - 19 Durrer D, Van Dam RTh, Freud GE, Janse MJ, Meijler FL, Arzbaecher RC. Total excitation of the isolated human heart. *Circulation* 1970;41:899-912.
 - 20 Wittkampf FHM, De Jongste MJL, Lie KI, Meijler FL. Effect of right ventricular pacing on ventricular rhythm during atrial fibrillation. *J Am Coll Cardiol* 1988;11:539-45.
 - 21 Grant RP. The mechanism of A-V arrhythmias with an electronic analogue of the human A-V node. *Am J Med* 1956;20:334-44.
 - 22 Lewis T. *The mechanism and graphic registration of the heart beat*. London: Shaw and Sons, 1925:377.
 - 23 Mackenzie J. The nature and significance of heart symptoms: II. The reflex process and the heart beat. *Br Med J* 1922;i:551-3.
 - 24 Mobitz W. Zur Frage der atrioventrikulären Automatie. *D Arch f klin Med* 1923;141:257-89.
 - 25 Dagget WM, Bianco JA, Powell WJ, Austen WG. Relative contributions of the atrial systole-ventricular systole interval and of patterns of ventricular activation to ventricular function during electrical pacing of the dog heart. *Circ Res* 1970;27:69-79.
 - 26 Clark AJ. Conduction in the heart of mammals. In: *Comparative physiology of the heart*. Cambridge: Cambridge University Press, 1927:49-51.
 - 27 Altman PL, Dittmer DS. *Biological handbooks: respiration and circulation*. Bethesda, Maryland: FASEB, 1971:278.
 - 28 Boineau JP, Moore EN. Evidence for propagation of activation across an accessory atrioventricular connection in types A and B pre-excitation. *Circulation* 1970;41:375-97.
 - 29 Dreifus LS, Haiat R, Watanabe Y, Arriaga J, Reitman N. Ventricular fibrillation. A possible mechanism of sudden death in patients with Wolff-Parkinson-White syndrome. *Circulation* 1971;43:520-7.
 - 30 Wenckebach KF, Winterberg H. *Die Unregelmässige Herzthätigkeit*. Leipzig: Wilhelm Engelmann, 1927:325-7.
 - 31 Van der Pol B, Van der Mark J. The heart beat considered as a relaxation oscillation and an electrical model of the heart. *Arch Neerl Physiol* 1929;14:418-43.
 - 32 Bethe A. Die biologische Rhythmus-Phänomene als selbständige bzw. erzwingene Kippvorgänge betrachtet. *Pflügers Arch f d ges Physiol* 1940;244:1-42.
 - 33 Van der Tweel LH, Meijler FL, Van Capelle FJL. Synchronization of the heart. *J Appl Physiol* 1973;34:283-7.
 - 34 Urthaler F, Katholi CR, Macy J, James TN. Mathematical relationship between automaticity of the sinus node and the AV junction. *Am Heart J* 1973;86:189-95.
 - 35 Katholi CR, Urthaler F, Macy J, James TN. A mathematical model of automaticity in the sinus node and AV junction based on weakly coupled relaxation oscillations. *Comp Biomed Res* 1977;10:529-43.
 - 36 West BJ, Goldberger AL, Rovner G, Bhargava V. Nonlinear dynamics of the heart beat. The AV function passive conduit or active oscillator? *Physica* 1985;17D:198-206.
 - 37 Schamroth L, Martin DH, Pachter M. The extrasystolic mechanism as the entrainment of an oscillator. *Am Heart J* 1988;115:1363-8.
 - 38 Cohen RJ, Berger RD, Dushane TE. Quantitative model for the ventricular response during atrial fibrillation. *IEEE Trans Biomed Eng* 1983;30:769-80.
 - 39 Van der Tweel I, Herbschleb JN, Borst C, Meijler FL. Deterministic model of the canine atrioventricular node as a periodically perturbed, biological oscillator. *J Appl Cardiol* 1986;1:157-73.
 - 40 Brody DA. Ventricular rate patterns in atrial fibrillation. *Circulation* 1970;41:733-5.
 - 41 Bootsma BK, Hoelen AJ, Strackee J, Meijler FL. Analysis of RR intervals in patients with atrial fibrillation at rest and during exercise. *Circulation* 1970;41:783-94.
 - 42 Kirsh JA, Sahakian AV, Baerman JM, Swiryn S. Ventricular response to atrial fibrillation: Role of atrioventricular conduction pathways. *J Am Coll Cardiol* 1988;12:1265-72.
 - 43 Langendorf R, Pick A, Katz LN. Ventricular response in atrial fibrillation: role of concealed conduction in the AV junction. *Circulation* 1965;32:69-75.
 - 44 Moore EN. Observations on concealed conduction in atrial fibrillation. *Circ Res* 1967;21:201-8.
 - 45 Dreifus LS, Mazgalev T. "Atrial paralysis": does it explain the irregular ventricular rate during atrial fibrillation? *J Am Coll Cardiol* 1988;11:546-7.
 - 46 Borst C, Meijler FL. Baroreflex modulation of ventricular rhythm in atrial fibrillation. *Eur Heart J* 1984;5:870-5.
 - 47 Meijler FL, Kroneman J, Van der Tweel I, Herbschleb JN, Heethaar RM, Borst C. Nonrandom ventricular rhythm in horses with atrial fibrillation and its significance for patients. *J Am Coll Cardiol* 1984;4:316-23.
 - 48 De Jongste MJL, Wittkampf FHM, Lie KI, Van der Tweel I, Meijler FL. Regularization of ventricular rhythm by right ventricular pacing in patients with atrial fibrillation [Abstract]. *Circulation* 1985;72(suppl III):32.
 - 49 Katz B, Schmitt O. Electric interaction between two adjacent nerve fibres. *J Physiol* 1940;97:471-88.
 - 50 Segers M, Lequime J, Denolin H. Synchronization of auricular and ventricular beats during complete heart block. *Am Heart J* 1947;33:685-91.
 - 51 Segers M. Les phénomènes de synchronisation au niveau du coeur. *Arch Int Physiol* 1946;54:87-106.
 - 52 Jalife J, Michaels DC. Phase-dependent interactions of cardiac pacemakers on mechanisms of control and synchronization in the heart. In: Zipes DP, Jalife J, eds. *Cardiac electrophysiology and cardiac arrhythmias*. New York: Grune and Stratton, 1985:109-19.
 - 53 Winfree AT. *When time breaks down. The three dimensional dynamics of electrochemical waves and cardiac arrhythmias*. Princeton, New Jersey: Princeton University Press, 1987.

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- 54 Jalife J, Moe GK. Effect of electrotonic potentials on pacemaker activity in canine Purkinje fibers in relation to parasystole. *Circ Res* 1976;39:801-8.
- 55 Jalife J, Moe GK. A biological model of parasystole. *Am J Cardiol* 1979;43:761-72.
- 56 Delmar M, Jalife J, Michaels DC. Effects of changes in excitability and intracellular coupling on synchronization in the rabbit sino-atrial node. *J Physiol* 1986;370:127-50.
- 57 Michaels DC, Matyas EP, Jalife J. Dynamic interactions and mutual synchronization of sinoatrial node pacemaker cells. *Circ Res* 1986;58:706-20.
- 58 Antzelevitch C, Jalife J, Moe GK. Electrotonic modulation of pacemaker activity. Further biological and mathematical observations on the behaviour of modulated parasystole. *Circulation* 1982;66:1225-32.
- 59 Waldo AL, Henthorn RW, Plump VJ, MacLean WAH. Demonstration of the mechanism of transient entrainment and interruption of ventricular tachycardia with rapid atrial pacing. *J Am Coll Cardiol* 1984;3:422-30.
- 60 Brugada P, Wellens HJJ. Entrainment as an electrophysiologic phenomenon. *J Am Coll Cardiol* 1984;3:451-4.
- 61 Winfree AT. Biological rhythms and the behavior of populations of coupled oscillators. *J Theor Biol* 1967;16:15-42.
- 62 Meijler FL. Atrioventricular conduction versus heart size from mouse to whale. *J Am Coll Cardiol* 1985;5:363-5.
- 63 Meijler FL. Comparative aspects of the dual role of the human atrioventricular node. *Br Heart J* 1986;55:286-90.
- 64 Meijler FL, Janse MJ. Morphology and electrophysiology of the mammalian atrioventricular node. *Physiol Rev* 1988;68:608-47.
- 65 Truex RC, Smythe MQ. Comparative morphology of the cardiac conduction tissue in animals. *Ann NY Acad Sci* 1965;127:19-33.
- 66 White PD, Kerr W. The heart of the sperm whale with special reference to the A-V conduction system. *Heart* 1915/1917;6:207-10.
- 67 James TN. Structure and function of the AV junction. *Jpn Circ J* 1983;47:1-47.
- 68 Scherf D. Retrograde conduction in complete heart block. *Dis Chest* 1959;35:320-1.
- 69 Winternitz M, Langendorf R. Auriculo-ventricular block with ventriculo-auricular response: report of six cases and critical review of the literature. *Am Heart J* 1944;27:301-21.
- 70 Schuilenberg RM. Patterns of V-A conduction in the human heart in the presence of normal and abnormal A-V conduction. In: Wellens HJJ, Lie KI, Janse MJ, eds. *The conduction system of the heart*. Leiden: Stenfert Kroese, 1976: 485-504.
- 71 Akhtar M, Damato AN, Batsford WP, Ruskin JN, Ogunkelu JB. A comparative analysis of antegrade and retrograde conduction patterns in man. *Circulation* 1975;52:766-78.
- 72 Shenasa M, Denker S, Mahmud R, Lehmann M, Gilbert CJ, Akhtar M. Atrioventricular nodal conduction and refractoriness after intranodal collision from antegrade and retrograde impulses. *Circulation* 1983;67:651-60.
- 73 Lehmann MH, Rehan M, Denkar S, Soni J, Akhtar M. Retrograde concealed conduction in the atrioventricular node: differential manifestations related to level of intranodal penetration. *Circulation* 1984;70:392-401.
- 74 Meijler FL. Latent pre-excitation: exposure of anterograde accessory pathway conduction during atrial fibrillation [Letter]. *Br Heart J* 1988;60:93-4.
- 75 Krikler DM, Rowland E. Concealed pre-excitation. *J Electrocardiol* 1978;11:209-11.
- 76 Milstein S, Klein SL, Rattes MF, Sharma AD, Yee R. Comparison of the ventricular response during atrial fibrillation in patients with enhanced atrioventricular node conduction and Wolff-Parkinson-White syndrome. *J Am Coll Cardiol* 1987;10:1244-8.
- 77 Fisch C, Knoebel SB. "Wedensky facilitation" in the human heart. *Am Heart J* 1968;76:90-2.
- 78 Scherf D, Schott A. *Extrasystoles and allied arrhythmias*. Chicago: William Heinemann, 1973: 252-4.
- 79 Oreto G, Satiello G, Luzzza F, Schamroth L. Electrotonic inhibition of an idioventricular escape focus by nonconducted sinus impulses. *Am Heart J* 1988;116:1097-9.
- 80 Saoudi N, Castellanos A, Galtier M, et al. Unusual electrocardiographic patterns of modulated parasystole. *Eur Heart J* 1987;8:1229-35.