

## Emergence of a New Paradigm in Understanding the Cardiovascular System: Pulse Synchronized Contractions

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### What We Will Show

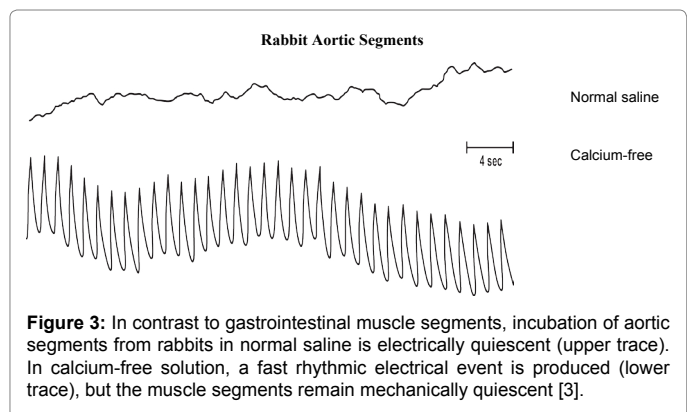
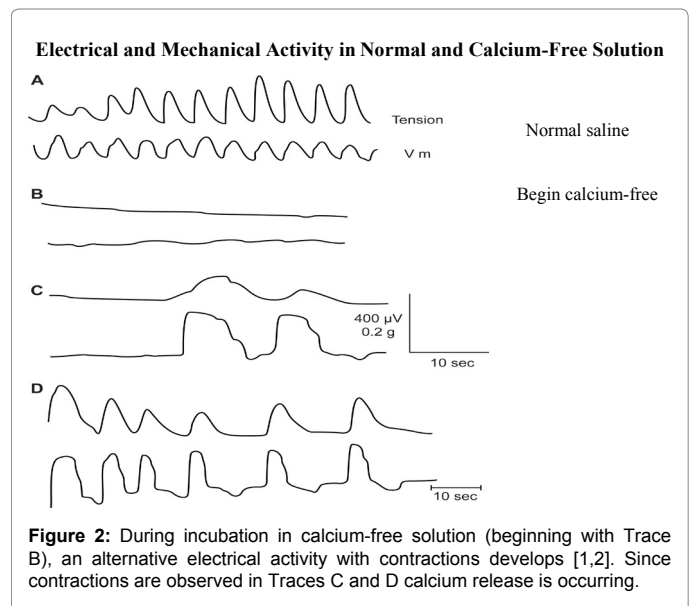
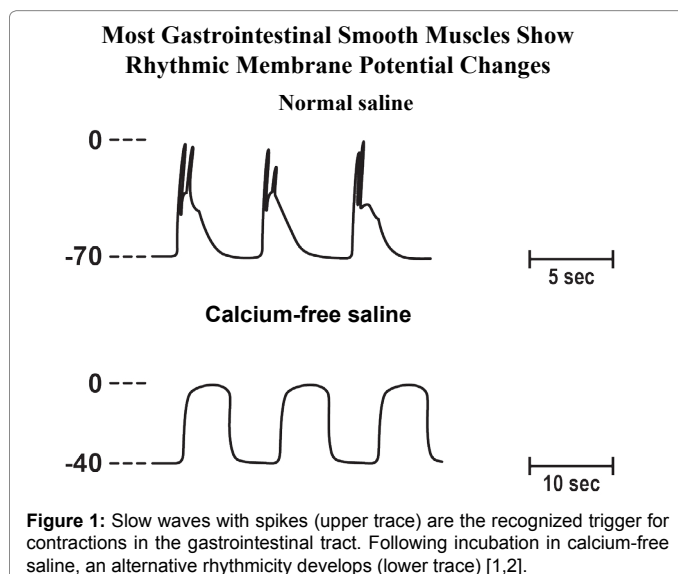
- The large conduit arteries undergo rhythmic smooth muscle activation in synchrony with the cardiac cycle.
- The contractions are neurogenic and are denoted as pulse synchronized contractions (PSCs).
- PSCs are not a movement artifact from the pulse wave or heartbeat.
- The pacemaker for the PSCs is in the right atrium.
- The smooth muscle wall of large arteries can contract as fast as the heartbeat.

### What Was Believed in Gastrointestinal Smooth Muscle

An increase in intracellular calcium activates contractions in muscle cells. Because smooth muscle cells are long, narrow-diameter cells, it was believed that an influx of calcium could serve as the sole source of activator calcium for contractions following changes in membrane potential. Therefore, no depolarization-mediated release of intracellularly stored calcium occurred (Figures 1-3).

### Windkessel Hypothesis: Otto Frank

- The prevailing hypothesis describing the behavior of the smooth muscle wall of the large arteries is that the wall does not contract in synchrony with the cardiac cycle but, rather, behaves as a passive elastic tube being rhythmically distended by pulsatile pressure changes. Neural input may modulate tone.
- Thus, it was believed that there was no vascular smooth muscle rhythmicity in synchrony with the cardiac cycle [4].



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## Proponents of the Windkessel Hypothesis Have Ignored

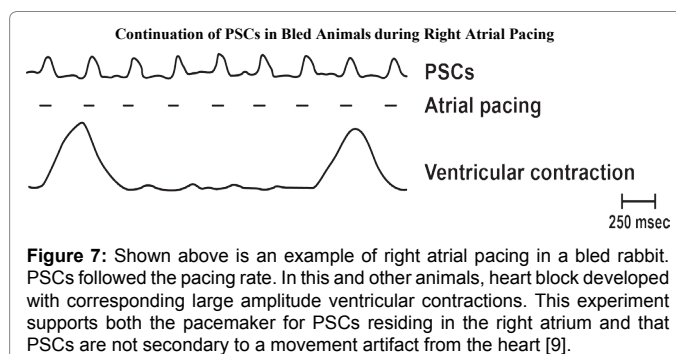
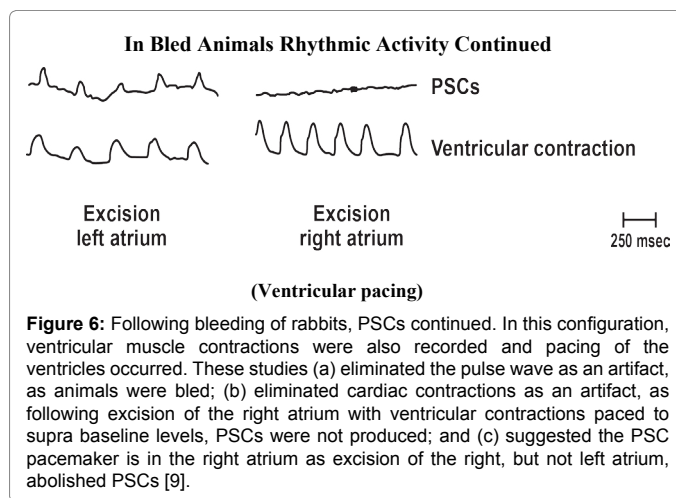
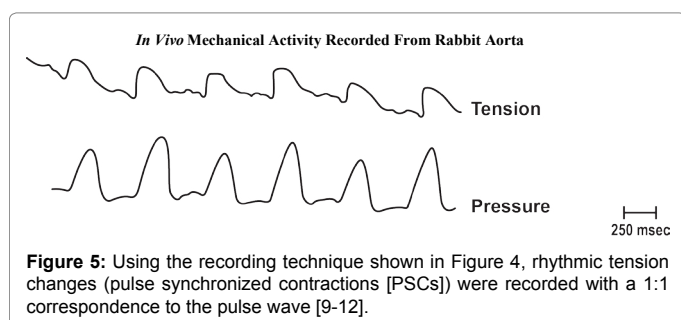
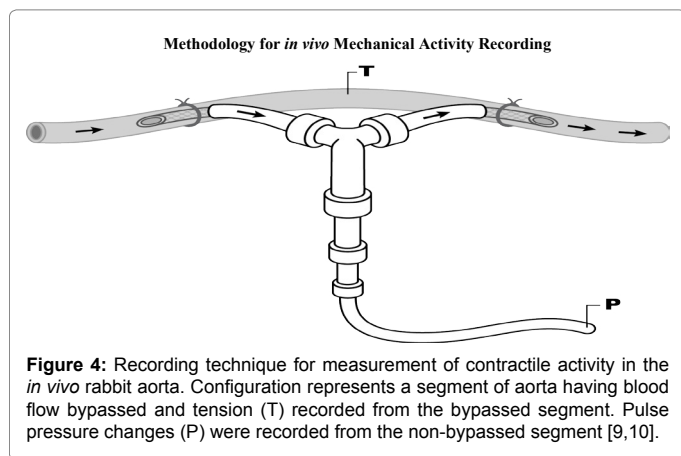
- Heyman, in a series of studies in man and dog that were published between 1955 and 1961 [5-8], showed:
  - » Extra-arterially recorded brachial pulses sometimes preceded intra-arterial pulses, suggesting arterial diameter varies in advance of pressure changes during the cardiac cycle.
  - » The difference between the extra-arterially recorded and intra-arterially recorded pulse waves was abolished by stellate ganglion block, suggesting a neurally mediated event.
  - » It was concluded that: “the behaviour of the artery in the pulse is contradictory to principles of passive elasticity but seem to provide evidence of active participation of the arterial wall...”
  - » This series of papers has been largely ignored.

## Hypothesis

Based on the ability of the aortic smooth muscle wall to generate fast rhythmic electrical activity in calcium-free solution (Figure 3), we sought to determine if the aortic smooth muscle wall could potentially show fast rhythmic contractile activity *in vivo* (Figures 4 and 5).

## Considerable Effort Was Expended Proving PSCs Were Not Due to a Mechanical Artifact

- Eliminate pulse wave (Figures 6 and 7)
- Eliminate cardiac contractility (Figures 6 and 7)
- Dispel prejudice that smooth muscle cannot “contract that fast” (Figure 8)



## Vessels Where PSCs Have Been Observed

Species	Vessel
Dog	Coronary, femoral, carotid arteries
Rabbit	Aorta
Cat	Pulmonary artery
Rat	Aorta
Human	Brachial artery

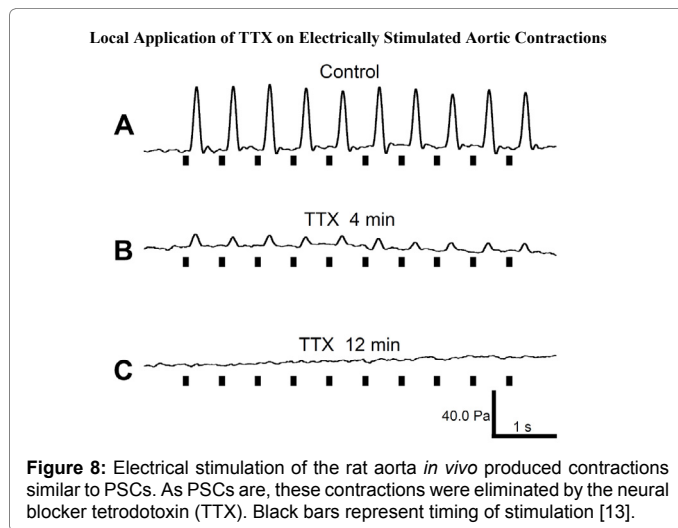
From references [5-13].

## PSCs

To evaluate whether the arterial smooth muscle wall is capable of contracting at the frequency of the heartbeat, electrical stimulation of the aorta *in vivo* was performed (Figure 8).

## Conclusion

- The smooth muscle wall of the large arteries is capable of undergoing rapid contractions (PSCs) at the rate of the heartbeat.
- The contractions are neurogenic in origin as evidenced by blockade by TTX or lidocaine [references 9-13] and are not secondary to movement artifacts from the pulse wave or heartbeat.
- The pacemaker for the PSCs is in the right atrium.
- Direct electrical stimulation of the nerves within the aorta yields similar contractile activity.



- PSCs represent a modified platform to understand the etiology of cardiovascular diseases allowing for the development of new therapeutic targets.
- PSCs have been recently reviewed [14,15].

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