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Method Article

# Modified Langendorff technique for mouse heart cannulation: Improved heart quality and decreased risk of ischemia

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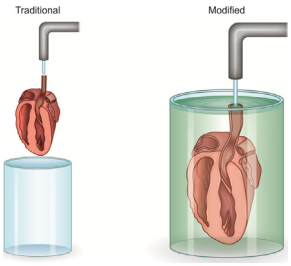
GRAPHICAL ABSTRACT




ABSTRACT

Oscar Langendorff introduced the first method for isolating a heart with contractile activity in 1895. Since then, the Langendorff method has remained a powerful technique in cardiac research and has led to major advances in medicine. The primary goal of the Langendorff method is to provide an isolated heart with oxygen and metabolites via a cannula inserted into the aorta. The Langendorff heart is a complex in vitro technique used primarily in pharmacological and physiological research that allows the evaluation of multiple cardiac hemodynamic parameters including, but not limited to, contractility and heart rate. This article will first provide a brief background of the Langendorff method as well as details regarding organ isolation. Finally, the article will discuss the benefits of a new technique for hanging the isolated heart aorta and the benefits of this technique over traditional methods



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## Method details

In the Langendorff preparation, the heart is first surgically removed from the animal's body. Subsequently, the aorta is suspended in the Langendorff apparatus and the heart is perfused via the aorta, usually with a nutrient rich oxygenated solution [Krebs and Henseleit solution (KHB)]. The delivery of nutrients and oxygen allows the heart to continue beating and also allows the evaluation of the effects of different drugs on the heart [1,2]. The Langendorff heart preparation relies on the constant pressure of the perfusion fluid to supply the myocardium with adequate oxygen and nutrients that may have been depleted during removal of the heart from the donor animal. The isolation of high-quality cardiomyocytes is critical for conducting successful experiments, and techniques for isolating murine heart cardiomyocytes are complex and time-sensitive. Major technical difficulties are related to the surgical procedures needed to cannulate the aorta to the Langendorff apparatus before starting the reperfusion. During this period, transient hypoxia and ischemia can cause damage to the heart, resulting in poor quality cells and affecting the results of the experiment [3]. The Langendorff method has led to many important advances in our understanding of ischemia–reperfusion injury, as well as cell based therapy and cardiac transplantation [4–12].

This article reviews the general principles of the Langendorff method and presents a novel modification of the Langendorff cannulation method that minimizes the effects of hypoxia and ischemia on experimental protocols. This method helps to produce high quality hearts for Langendorff experiments investigating cardiac parameters and ventricular myocytes.

## Principles of the Langendorff method

Most isolated perfused heart preparations are based on the method originally described by Langendorff [13]. Once the heart is removed from an anesthetized animal it is clipped to a cannula on the perfusion apparatus. The cannula is attached to the outflow of a reservoir containing an oxygenated perfusion solution. The majority of research protocols use a physiologic salt solution that mimics the content of plasma (KHB) that is delivered at 37 °C with physiological pH of 7.4 [14–16]. In each Langendorff experiment, a wide range of physiological, morphological, and pharmacological parameters, including contractile function, heart rate, cardiac metabolism, and electrical activity of the heart, can be evaluated. Another advantage of this technique is that the intact organ will spontaneously beat when place in an environment with the proper oxygenation, perfusion fluid, and temperature, making this method reasonably physiological. Moreover the heart is free from the influence of other organs, the systemic circulation, and signals from the central and autonomic nervous systems [17]. The Langendorff technique allows for the induction of ischemia, arrhythmia, and hypoxia to various degrees, which makes it a unique tool for the study of pathological cardiac conditions. The isolated heart preparation is valuable in studying the mechanisms underlying arrhythmias as well as ischemia-reperfusion. The model is also a valuable tool for studying the direct effect of drugs on the heart including cardiotoxicity. Additionally, a wide range of measurements can be done with the isolated heart to evaluate the mechanisms of acute cardiotoxicity [18]. Importantly, it should be noted that the potential disadvantages of the Langendorff isolated perfused heart technique are highly dependent on the skills of the investigator. The heart is vulnerable to contusion injuries, and there is a significant possibility of ischemic damage to the heart during its isolation and instrumentation. Improper preparation has been reported to have a great impact on the initiation and maintenance of ischemia-induced ventricular fibrillation in isolated rabbit hearts, making them less suitable for study [19]. Among different animal species, the isolated mouse heart preparation is more complicated because of its high heart rate and small size. The guinea pig heart, having extensive collaterals in the coronary circulation, is not suitable for ischemia studies [15,20].