# NOVEL DESIGN OF A FRANK-STARLING PHYSIOLOGICAL MOCK CIRCULATORY LOOP FOR IN-VITRO TESTING OF ROTARY BLOOD PUMP

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## ABSTRACT

Introduction: Frank-Starling mechanism (FSM) is a significant physical control of the native heart, this study focuses on the development of mock circulatory loop (MCL) that mimic the FSM to assess the performance of rotary blood pump (RBP).

Materials and Methods: Bellow pump was newly designed to generate the left ventricular contraction via the hydraulic MCL. The FSM of MCL was developed based on the time-varying elastance curve. First, the real time response of changes in preload, afterload and contractility were employed to validate the FSM performance of MCL. The maximal elastance (Emax) was varied from 1.1 to 1.9 mmHg/ml, covered range of normal and abnormal heart. Second, RBP was inserted into MCL and was altered pump speed from 1k to 3k with a steps of 200 rpm. The Pressure-Volume loop (PV) was created both with and without RBP.

Results: The end diastolic volume (EDV) and the stroke volume (SV) calculated from PV loop decreased during decrease preload. For increased afterload, PV loop showed the increment of end systolic pressure (120±4.8 to 188±1.25 mmHg) in contrast with the reduction of SV (72±0.85 to 63±0.33 ml). The resulting of PV loop and the regression line at the setting of Emax were closely mimicked (R2=0.98). For different levels of RBP support, PV loops represented change in FSM similar to in vivo test.

Conclusion: This study demonstrated the capability of novel MCL that can represent the FSM in similar to physiological cardiac response during RBP support.

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**Keywords:** Frank-Starling mechanism, mock circulatory loop, rotary blood pump

## 1. INTRODUCTION

Cardiovascular disease is one of the top leading causes of death in Thailand and other countries [1]. Its mortality rate is increasing year by year.

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Since this disease damages the function of the heart, it is also one of the leading causes of heart failure. Patients who are suffering with the end-stage heart failure are normally treated by heart transplantation. However, they have to wait for a suitable heart that limited by the number of heart donors. To compensate this limitation, rotary blood pumps (RBP) was developed to be the alternative therapy provided for internal and external circulatory supports [2]. For heart failure patient, RBP is composed of cardiac device known as ventricular assist device. Another support, RBP is applied to be an important component of the cardiac support device that is introduced into the routine surgery including heart lung machine and extracorporeal membrane oxygenation (ECMO) [3].

Several accomplished RBPs are required the in vitro evaluation of their performance before clinical trials are conducted. Mock circulatory loops (MCL), a simulation of the cardiovascular circulatory system, provide a suitable platform for testing the cardiovascular devices. Previous development of testing devices have been created as the basic conceptual loop ,which consists of resistant valve, reservoirs, flow meter and pressure transducers [4,5]. However, this simulation provided insufficient evidence to determine the hemodynamic responses generated by RBP because this system just operated the static flow. Hence, the pulsatile duplication has been developed to overcome this situation [6-17]. Although many MCL has been developed including many cardiac circulatory characteristics such as pulmonary circulation, fluid inertia and variance compliance. However, the response of Frank Starling law did not often take into consideration. Until now, many researchers have developed the mock circulatory system adhere to Frank-Staling mechanism to improve the potential simulation of the circulatory system. There are many algorithms that have been introduced to simulate this mechanism. In 1994, Jeffrey et al., [18] developed the MCL that provided the simulation of systemic circulation on which automatic control algorithm based upon elastance control loop. However, this research studied only the effect of increased systemic resistance on PV loop. In 2001, Balao et al., [19] conduced the elastance-based control of MCL. This MCL was implemented by the hydraulic system. A stainless-steel bellows was employed to simulate a pattern of left ventricular volume by varying a position. The ventricular contraction with responses by time has been represented by a time-varying elastance. The maximal value of elastance was located at the point of end systole.

Therefore, it indicated the capable of varying ventricular contractility. As result, this design was able to simulate changes in preload, afterload, and contractility in similar to natural heart. Moreover, the result demonstrated that external work increased linearly with stroke volume (SV) whereas models a Frank-Starling Mechanism. Thus, this system was enabled to use as a new tool for evaluation of the cardiac devices such as LVAD. Nevertheless, a systematic system both compliances and resistance were simulated by manually adjusted [19].

In the current study, the novel design of the MCL for evaluating the hemodynamic effect on RBP in respects to Frank-Starling mechanism was developed. The MCL simulated the systemic circulatory system via the hydraulic environment. This featured the simulation of left ventricular contraction by using the novel design of ventricular simulator, known as the bellow pump. The Frank-Starling mechanism was implemented by using a numerical elastance model to control the LV contraction. The elastance function was real time derived from both LV pressure and volume of MCL to control the LV contraction. To validate the performance of MCL, the hemodynamic response during changes in preload, afterload and contractility in similar to the Frank-Starling mechanism of the native heart were instantaneously varied. The hemodynamic effects both with and without RBP were investigated.

## 2. MATERIALS AND METHODS

### 2.1 Configuration of MCL

The new design of MCL provided a left ventricular (LV) contraction and allowed to select the physiological parameters. This system was physically divided into 3 main segments: cardiac segment, including left atrium (LA) and left ventricle (LV); vascular section, involving the aortic compliance (AoC) and total peripheral resistance (TPR); and rotary blood pump (RBP). A configuration of the MCL is shown in Fig.1.

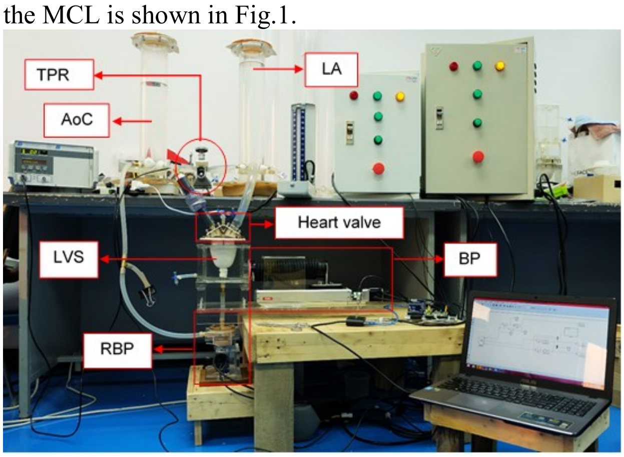


**Figure 1.** Configuration of mock circulatory loop consisted of arterial compliance (AoC), atrial reservoir (LA), left ventricular sac (LVS), bellow pump (BP), rotary blood pump (RBP), total peripheral resistance regulator (TPR), aortic and mitral valve (Heart valve).

### 2.2 Cardiac segment

Atrial reservoir was used to collect the water before fed into the left ventricle and to prepare the preload pressure. This was fabricated by the acrylic cylinder reservoir. At the top of this reservoir was opened to the air. Hence, the level of water inside this reservoir can be used to provide the desired atrial pressure as well as the preload.

The design of artificial left ventricle was purposed to mimic the anatomical shape of natural ventricle for simulating LV compliance during systole and diastole. The silicone rubber (RTV 3483, XIAMET ER, California) was introduced to fabricate the sack of left ventricle. The LV sack was designed as the shape of half ellipsoid with an inner diameter of 64 mm, a thickness of 6 mm, and the unstretched volume of 150 ml. This was anatomically represented the same size as the literature review of the native left ventricle [20,21]. For the bottom of LV sack, an apex was designed to connect with the inlet flow port of RBP. For the top of LV sack, this was designed to place inside the sealed chamber. The sealed chamber of water contained 4 connectors. Two connectors were designed as a V shape to provide the anatomical location for placing heart valves: mitral and aortic valve, which was simulated by 12.7 mm (1/2 inch) of a clear PVC swing check valve (S1520C05, Spears, California). Another connectors were provided to adjoin with ventricular simulator (bellow pump) and RBP.

### 2.3 Ventricular simulator

The behavior of left ventricle was implemented by using the hydraulic system. The sealed chamber mounted with LV sack was connected to the new design of ventricular simulator, called as bellow pump (BP). The BP was a combination between a rubber bellow (SERVICE-KIT 900-222, SACHS, Germany) and the linear actuator: AC motor (R2AA04010FXH00W, SANYO DENKI, Japan) coupled with a linear motion guide (KRF5-10-0150-0-AQ, THK, Tokyo). The action of left ventricle was archived by change in length of a rubber bellow. During ejecting phase, the LV sack was collapsed by transferring the compressive force generated by contracting the rubber bellow and thus the pressure inside LV sack became higher (Fig.2A). During relaxation, a rubber bellow was rapidly retracted and thus reduced the LV pressure (Fig. 2B). Thus, the intensive LV contraction and relaxation could be modified by varying the length of bellow and moreover the speed time earned for achieving these events could be used to adjust the desired heart rate.

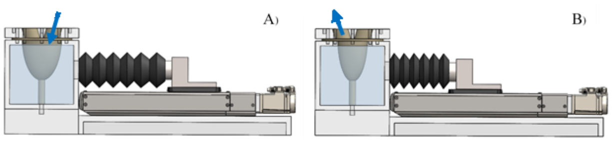


**Figure 2.** Configuration of bellow during left ventricular relaxation (A) and contraction (B).

### 2.4 Ventricular section

The simulation of arterial or aortic compliance produces a vascular characteristic. This was created by using the acrylic cylinder reservoir same as the atrial chamber. At the top of this chamber, it was completely closed from the environment and thus could be adjusted the compliance by mean of the compressive air above water contained inside the chamber.

The adjustment of the total peripheral resistance in the simulation of the systemic circulation was used to adjust the afterload, which is the load acting on the ventricle during contraction. This implemented by squeezing the 25.4 mm (1 inch) of the tube located between the arterial compliance and the atrial reservoir.

### 2.5 Rotary blood pump

External RBP that was subjected to in vitro performance test under this MCL have been developed by Wannawat P, and Foojinphan N [22]. This design consisted of the impeller, housing and driving unit. The impeller and housing (Fig.3) were constructed by using a 3D printer with a dental material (MED670-VeroDent, Stratasys Ltd., United Stated), which has an excellent strength and durability. The method employed to drive this impeller was magnetically-driven. The magnetically driving feature (Fig.4) involved the impeller and magnet base that were combined with 8 pieces of magnetic slices. The magnet base was mounted to the shaft of motor so that the impeller could be rotated via the mechanism of magnetic coupling pump.

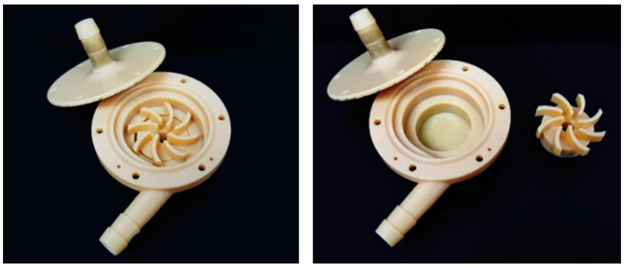

**Figure 3.** Configuration of impeller and housing.

### 2.6 Data acquisition system

The data acquisition (Fig. 5.) could be divided into 2 main parts. First, the input data signals consisted of the LV pressure (LVP), LV volume (LVV), aortic pressure (AOP), aortic flow (AOF) and pump flow (Q). Another part was the output data signal used to control the RBP speed and the BP.

Input; the measurement of AOF were obtained by clamping with the ultrasonic flow sensor (9PXL, Transonic System Inc., USA) and monitored by using the tubing flow module (TS410, Transonic System Inc., USA). In case of pressure measurements, the signals were recorded by the fluid fill pressure sensors (TruWave Disposable Pressure Transducer, Edward Medical Inc., USA) combined with the signal converters. All measurements were connected to NI USB-6009 (14-Bit, 48 kS/s Low-Cost Multifunction DAQ, National Instruments Corporation, Texas) and were transferred signals to the MATLAB / SIMULINK (The Mathworks, Natick, MA, U.S.A.) environment via USB port. A prototyping visual software tool in SIMULINK was used to digitize these data with the selected sampling frequency of 200 Hz. Another hemodynamic parameter, the LV volume was achieved by converting the number of different length in rubber bellow converted from motor encoder of BP. The motor encoder of BP was implemented by using the AC servo systems with EtherCAT interface (SANMOTION R-ADVANCED MODEL, SANYO DENKI, Japan) and was transferred to SIMULINK environment via serial communication.

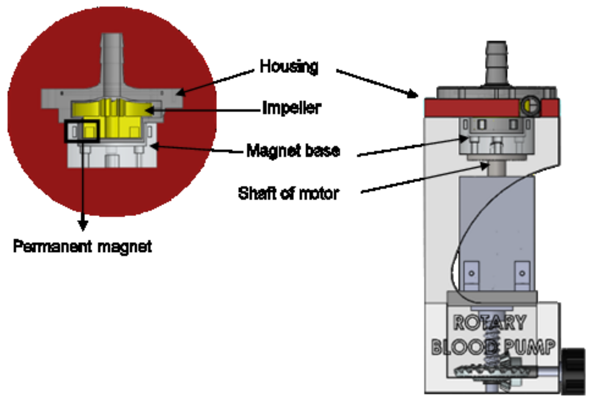


**Figure 4.** The driving feature of RBP.

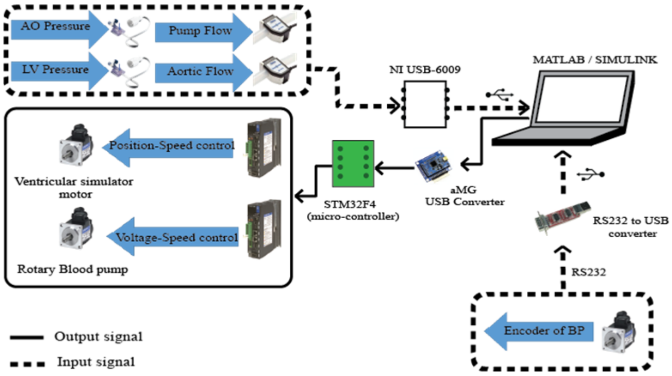


**Figure 5.** Communication system of mock circulatory loop; AO, aortic; LV, left ventricular; BP, bellow pump; RBP, rotary blood pump.

Output; the micro controller (STM32F4 discovery, STMicroelectronics, Switzerland) combined with the USB converter (AMG USB Converter – N, Aimagin, Thailand) was used to control the BP and RBP speed. The SIMULINK simulation model with the WAIJUNG block set (Aimagin, Thailand) was chose to process this communication at the high-speed baud rate of 5MHz. The speed of BP, which was used to determine heart rate, was adjusted by altering the frequency of the pulse signal generated from SIMULINK blockset. The state of LV behavior: contraction and relaxation, was regulated by switching the rotational direction of BP.

### 2.7 Elastance control system

The elastance template, which is the proportional between LVP and LVV, was used to simulate the FSM. The input hemodynamic templates of LV volume and pressure of patient who was suffering with myocardial infarct served from Liang Zhong et al [26] were used to calculate the reference elastance template by using an equation below:

$$e_{ref}(t) = \frac{P_{ref}\ (t)}{V_{ref}\ (t)} \tag{1}$$

Whereas $e_{ref}(t)$ is the time-varying reference elastance, $P_{ref}\ (t)$ is pressure reference and $V_{ref}\ (t)$ is a volume reference

This system could be divided into 2 feedback loops: volume feedback loop and elastance feedback loop, as shown in Fig.6. First, the volume feedback loop was used for driving a bellow pump to follow the reference volume curve. For the elastance feedback loop, the instantaneous elastance, which is a proportional between LVP and LVV measured from MCL, was calculated in real time and was used as the negative feedback signal to determine the error between this result and the reference elastance. To compensate the control system, the proportional-integral controller (PI) was employed.

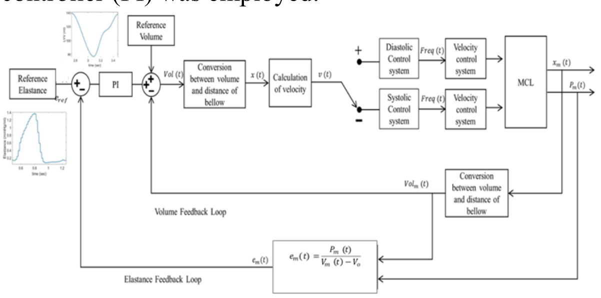


**Figure 6.** The elastance based control block diagram. $e_{ref}(t)$ is the elastance reference waveform, Vol(t) is the desired left ventricular volume, x(t) is the desired position of bellow, v(t) is the desired velocity, Freq(t) is the frequency of the square wave, $x_m$ (t) is the measured displacement of bellow, $V_m$ (t) is the measured left ventricular volume, $P_m$ (t) is the measured left ventricular pressure and $e_m$ (t) is the elastance calculated.

### 2.8 Experimental setup

The Initial experiment of MCL was the setup of MCL without the connection of RBP. To archive this require, a connecting tubes that linked between the apex of LV sack and the inflow of RBP, and between the outflow of RBP and the arterial compliance were clamped. This experiment was used to validate the performance of MCL in responses to FSM. To implement this validation, the real time responses of MCL during changes in preload, afterload and contractility were assessed. The maximal elastance ($E_{max}$) was varied from 1.1 to 1.9 mmHg/ml with four different steps, covered range of normal and abnormal heart. This variation was used to validate the ability of MCL in response to change in contractility by means of the linear regression of the end diastolic pressure volume relationship ESPVR. Four different Emax were achieved by scaling the reference elastance template, as shown below:

$$e_n(t) = k \times e_{ref}(t) \tag{2}$$

Where:

$e_n(t)$ is the new template of the elastance function, mmHg/ml. $k$ is the compliance scale factor, varied from $0.8 \le k \le 1.4$. $e_{ref}(t)$ is the original template of the elastance function, mmHg/ml.

For experimental evaluation of RBP, the RBP was placed between the apex of LV sack and the arterial compliance. The clamps on the inflow port and outflow port of RBP were released. The RBP speed was gradually increased from 1300 to 2800 rpm with 8 steps in parallel to the operation of MCL. The measured hemodynamic parameters were recorded through the workspace of MATLAB in real time.

## 3. RESULTS

### 3.1. Initial Experiment

The result obtained from initial experiment of MCL without any changes in cardiac conditions represented the constant SV of 60 ml which was similarly to the input signal of LVV. Although, the LVV measured from MCL showed the same shape as the input signal, the abnormal node obtained during filling phase was performed and can be noticed in a circular dotted line on Fig.7A. For the response of LVP, the values was 120/80 mmHg with the cardiac output of 1.5 l/min indicated the abnormal heart. The hemodynamic responses including LV pressure, LV volume, and aortic pressure are shown in Fig.7B.

In case of change in preload at the constant $E_{max}$ from database (1.36 mmHg/ml; k=1), the height of the water level in atrial reservoir was varied. Fig.8A shows the comparison of the pressure and volume in response of change in preload. As a result, the EDV decreased from 131±1.8 to 104±1.8 ml ($p<0.01$) as well as the 8% of SV decrease during reduction of preload and moreover these results could be determined on the P-V loop (Fig.9A).

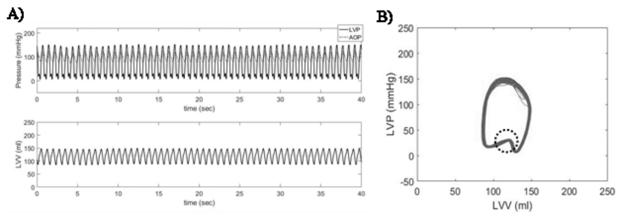


**Figure 7.** Hemodynamic responses including left ventricular pressure (LVP), aortic pressure (AOP) and left ventricular volume (LVV) (A) and P-V loop (B) with abnormal node (circle dotted line).

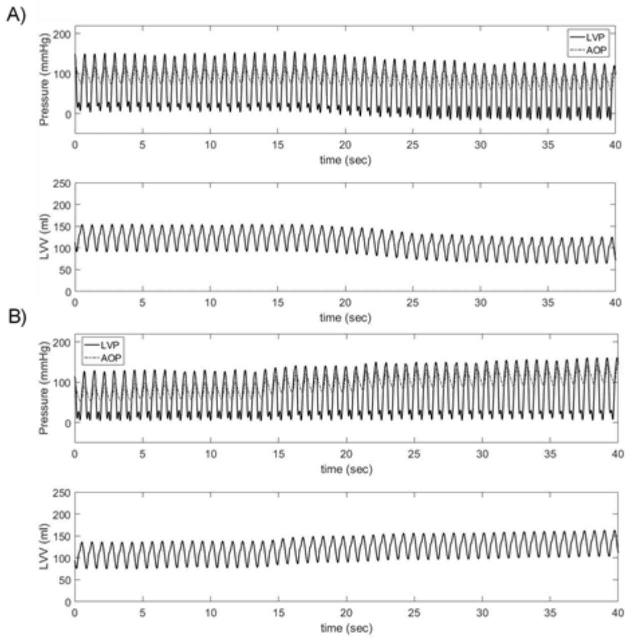


**Figure 8.** Hemodynamic responses in response to changes in preload (A) and afterload (B) including left ventricular pressure (LVP), aortic pressure (AOP) and left ventricular volume (LVV).

For afterload validation at the constant $E_{max}$ from database, the TPR was altered by gradually changing the diameter of tube located between arterial compliance and atrial reservoir. Fig.8B shows that both of LVP and AOP measured from MCL increased in contrast to ESV. The reduction of ESV could be determined by the feature of P-V loop in Fig.9B. The result of P-V loop demonstrated that the ESV suddenly raised from 120±4.8 to 188±1.25 mmHg ($p<0.01$), in contrast, the reduction of SV varied from 72±0.85 to 63±0.33 ml ($p<0.01$).

Fig. 9C shows the response of P-V loop during varying contractility. ESPVR, which is the linear line at the $E_{max}$, is indicated by the dotted line on this diagram. This line was remarked that the increment of contractility leaded to increase the ESPVR. The linear regression of ESPVR ($R^2=0.95$) was shown in Table 1. This table also compared between the setting of maximal elastance and the slope of ESPVR obtained from MCL.

### 3.2 Experimental result of MCL with RBP

The complete MCL was used to evaluate the performance of RBP on the FSM. The RBP speed was altered from 1300 rpm to 2800 rpm with 8 steps. The effect of RBP speed increase on pressure, including LVP and AOP, and LVV are shown in Fig.10A. The LVP increased with increasing the RBP speed until RBP speed reached 2500 rpm. At the RBP speed above 2500 rpm, LVP reduced. The AOP invariably increased as RBP speed stepped up. The P-V loops of MCL without RBP support and MCL with RBP support are shown in Fig.10B. The area of P-V loop became smaller when the RBP speed above 2500 rpm. This event also reduced the SV. The EDV reduced nearly zero while Emax was constant. Fig.11 shows the effect of RBP speed on the fluid flow, including aortic flow (AOF) and pump flow (Q). The AOF decreased till zero when the RBP speed reached 2200 rpm. In contrast, the mean of Q produced by RBP increased from 0.6 to 2.6 l/min and also presented the reduction of its peak to peak.

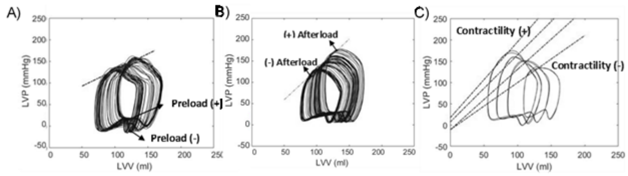


**Figure 9.** Pressure-Volume loop from MCL in response to changes in preload (A), afterload (B) and contractility (C).

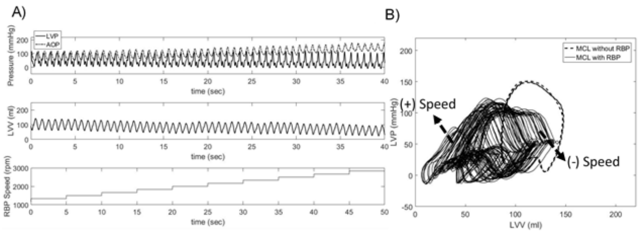


**Figure 10.** The hemodynamic effect including left ventricular pressure (LVP), aortic pressure (AOP) and left ventricular volume (LVV) of RBP speed increase (1300 to 2800 rpm).

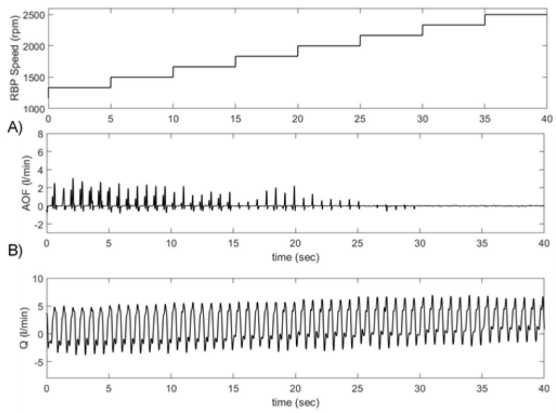


**Figure 11.** Configuration of fluid flow in response to change in RBP speed including aortic flow (AOF) and pump flow (Q).

## 4. DISCUSSION

The MCL with a new design of ventricular simulator, bellow pump, was able to mimic Frank-Starling cardiac mechanism and thus represented the hemodynamic responses in a nearly circulatory physiology. The ESPVR obtained from changes in preload and afterload remained constant, similar to cardiac physiology [18-28]. The MCL in response to changes in preload demonstrated that the SV is increased during increasing the EDP, similar to Frank-Starling response [18,19,24]. The afterload validation showed that the ESV was inversely proportional to the SV. This result represented that the cardiac output decreased when the contractility of myocardial remained constant, similar to the resulted obtained from in-vivo test [28]. According to a result obtained from MCL with change in contractility, the ESPVR was instantly increased as the maximal elastance template increased. This result demonstrated that increased contractility also increased SV like the native cardiac physiology [23] and thus represented in the same way as the in-vivo test [24]. In addition, the results of MCL in respects to change in contractility during varying afterload were physiologically presented. The slopes calculated from the linear regression of ESPVR in each contractility (R2>0.95) setting, as shown in Table 1, demonstrated that the MCL could be used to mimic both of normal heart (1.6≤Emax≤1.3) and heart failure (Emax≤1.3) [23-25].Therefore, the MCL was able to simulate cardiac mechanism and thus could produce the hemodynamic response in similar to the native heart.

The cardiac response including Frank-Starling mechanism was simulated to investigate the performance of RBP. The impact of FSM on the mechanism of RBP in this MCL was successfully operated similar to the literature reviews [7,8,11,12]. During RBP speed increase, LVP reduced because of change in preload (Fig. 4.35), which is produced from FSM [12,28]. The flow through the aortic valve (Fig.4.38) also decreased due to the reduction of SV and the effect of LV unloading [12]. Thus, the closed aortic valve could be occurred in case of full support and can lead to an abnormal aortic valve, either stenosis or regurgitation [29,30]. The reduction of SV and the closed aortic valve could affect the LV suction. Moreover, these results also had an impact on the feature of pump flow. The pump flow increased and represented the reduction of its peak to peak while RBP speed is higher. This result showed the same response to the in vivo test [31] and also demonstrated that the SV decreased while the support level increased. This represented how the increased RBP speed impact on the native cardiac function, as summarized in Fig.12. Although the complete MCL can be used to simulate the Frank-Starling mechanism, this MCL simulated only the systemic circulation. Thus any effect of RBP on pulmonary circulation was not investigated. In addition, the total peripheral resistance and the arterial compliance were manually adjusted by user. Therefore, the auto adjustment of these parameter was not implemented. Moreover, the fluid that was used in this circulation did not mimic the property of blood such as the viscosity. Thus, the hemodynamic response obtained from this MCL may be showed the different value from the real environment of heart. For the future development, According to the limitation of this MCL, the simulation of pulmonary circulation could be performed to investigate the performance of RBP for both systemic and pulmonary circuit. Moreover, the auto regulation of total resistance, compliance and heart rate should be included into the control system to improve the capability of the human circulatory simulation.

**Table 1 Afterload response of four contractility**

| $E_{max}$ Setting | Slope | Accuracy % | y-intercept | $R^2$ |
|---|---|---|---|---|
| 1.091 (k=0.8) | 1.110 | 98.258 | -11.772 | 96.840 |
| 1.364 (k=1.0) | 1.421 | 95.797 | -11.830 | 96.010 |
| 1.636 (k=1.2) | 1.562 | 95.464 | 7.998 | 96.050 |
| 1.909 (k=1.4) | 1.786 | 93.553 | 16.476 | 98.750 |

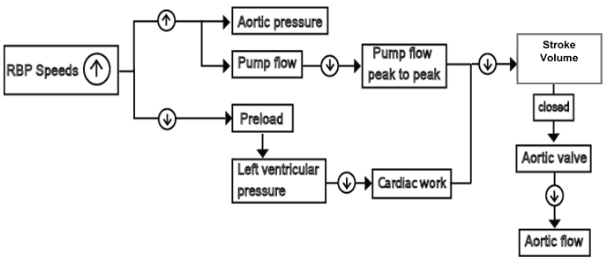


**Figure 12.** The effect of higher RBP speed on the cardiac response obtained from MCL with EBS.

## 5. CONCLUSION

The developed MCL successfully simulated the Frank-Starling mechanism. The hemodynamic parameters in response to changes in preload, afterload, and contractility were similar to the native heart. Due to a good reproducibility of the mock circulatory loop, its capability performs an actual cardiac physiological response during cardiac assist device support. Hence, this mock circulatory can be used to get better understanding of the interaction between the human circulatory system and RBP mechanism and thus can help to improve the performance of RBP before available in clinical trial.

## REFERENCES

[1] P. Laothavorn, K. Hengrussamee, R. Kanjanavanit, W. Moleerergpoom, D. Laorakpongse, and O. Pachira, et al. "Thai Acute Decompensated Heart Failure Registry (Thai ADHERE)", CVD Prevention and Control. pp 89–95, 2010
[2] WebMD.com [Internet]. WebMD, LLC. 2005-2016. Advances in Heart Failure Treatment. Available from: http://www.webmd.com/heart-disease/heart-

failure/features/lvad-end-stage-heart-failure-new-advances-in-treatment#1.
[3] H.G. Wood, A.L. Throckmorton, A. Untaroiu, and X. Song., "The medical physics of ventricular assist devices". Rep Prog Phys. vol.68, pp 545–576, 2005.
[4] K. Makinouchi, and Y. Ohara. "Internal hydraulic loss in a seal-less centrifugal Gyro pump", Artificial Organs, vol.18, no.1, pp 25-31, 1994.
[5] M. Yoshino, M. Uemura, K. Takahashi, N. Watanabe, H. Hoshi, and Ohuchi, et al. "Design and evaluation of a single-pivot supported centrifugal blood pump", Artificial Organs vol.25, no.9, pp 683-687, 2001.
[6] L.N. Scoten, D.K. Walker, and Brownlee. R.T. "Construction and evaluation of a hydro mechanical simulation facility for the assessment of mitral valve prostheses", J Med Eng Technol., vol. 3, no. 1, pp 8-11, 1979.
[7] G.M. Pantalos, S.C. Koenig, K.J. Gillars, G.A. Giridharan, and D.L. Ewert., "Characterization of an adult mock circulation for testing cardiac support devices", ASAIO J., vol.50, no.1, pp 37-46, 2004.
[8] Y. Yokoyama, O. Kawaguchi, T. Shinshi, U. Steinseifer, and S. Takatani. "A new pulse duplicator with a passive fill ventricle for analysis of cardiac dynamics". J Artif Organs, vol.13, pp189–196, 2010.
[9] T. Khienwad, and P. Naiyanetr. "Effect of tubing length pump on flow derived index during rotary blood pump suppor", Conf Proc lASTED. pp. 270-276, 2017.
[10] D .Timms, Design, "Development and evaluation of centrifugal ventricular assist devices.", Queensland University of Technology 2005
[11] D .Timms, S.D. Gregory, N.A. Greatrex, M.J. Pearcy, J.F. Fraser, and U. Steinseifer., "A Compact mock circulation loop for the in vitro testing of cardiovascular devices",. Artificial organs; vol.35, no.4, pp 384-391, 2011.
[12] S-H Jansen-Park, M.N. Mahmood, I. Müller, K.L. Turnhoff,, T. Schmitz-Rode, and U. Steinseifer., et al. "Effects of interaction between ventricular assist device assistance and autoregulated mock circulation including Frank-Starling mechanism and baroreflex", Artificial Organs., vol.40. no.10, pp.981-991, 2015.
[13] T. Khienwad , P. Wannawat, and P. Naiyanetr, "Assessment of artificial heart valve using dynamic mock circulatory system". IJABME. vol.9, no.1, pp 21-26, 2016.
[14] T. Khienwad, "Development mock circulatory system for testing function of valve", Bachelor Thesis, Mahidol University, 2015
[15] C.S. Jhun, J.D. Reibson, and J.P. Cysyk. "Effective ventricular unloading by left ventricular assist device with stage of heart failure: Cardiac stimulator study", ASAIO J., vol.57, no.5, pp 407-413, 2011.
[16] F.M. Colacino, F. Moscato, F. Piedimonte, G. Danieli, S. Nicosia, and M. Arabia., "A modified elastance model to control mock ventricles in real-time: numerical and experimental validation", ASAIO J., vol.54, no. 6, pp.563-573, 2008.
[17] S. Schampaert, K.A. Pennings, M.J. van de Molengraft, N.H. Pijls, F.N. van de Vosse, and M.C. Rutten. "A mock circulation model for cardiovascular device evaluation", Physiol Meas., vol.35, no.4, pp.687-702, 2013.
[18] L.W. Jeffrey, F.A. James, and JR Boston, et al. "Load sensitive mock circulatory system for left ventricular assist device controller evaluation and development". Eng Med Biol Soc., pp 89-90, 1994.
[19] L.A. Baloa, J.R. Boston, and J.F. Antaki., "Elastance-based control of a mock circulatory system", Ann Biomed Eng., vol.29, pp. 244–251, 2001.
[20] M.L. Roberto, B. Michelle, and B.D. Richard, et al. "Recommendations for chamber quantification", Eur J Echocardiography., vol.7, pp. 79-108, 2006.
[21] M. Bayraktar, and J. Männer., "Cardiac looping may be driven by compressive loads resulting from unequal growth of the heart and pericardial cavity"., Front Physiol., vol.5, pp. 112, 2014.
[22] P. Wannawat and N. Foojinphan., "Development of external centrifugal blood pumps with pulsatile flow"., Bachelor Thesis, Mahidol University, 2016
[23] C. Guyton, and E. John., "Guyton Textbook of Medical Physiology. 11th ed." China. Elsevier Inc; 2006.
[24] H. Suga, and K. Sagawa., "Instantaneous pressure-volume relationships and their ratio in the excised, supported canine left ventricle", Circ Res., vol. 35, no.1, pp.117-26, 1974.
[25] L .Zhong, D.N. Ghista, E.Y. Ng, and S.T. Lim. "Passive and active ventricular elastances of the left ventricle". Biomed Eng Online., vol.4, no.10, 2005.
[26] W.L. Maughan, K. Sunagawa, D. Burkhoff, and K. Sagawa., "Effect of arterial impedance changes on the end-systolic pressure-volume relation", Circ Res., vol.54, no.5, pp595-602, 1984.
[27] H .Suga, "Time course of left ventricular pressure-volume relationship under various end-diastolic volumes", Jpn. Heart J. vol.10. pp. 509–515, 1969.
[28] K. Fukamachi, A. Shiose, A. Massiello, D.J. Horvath, L.A. Golding, and S. Lee, et al. "Preload sensitivity in cardiac assist devices", Ann Thorac Surg., vol.95, no.1, pp.373-80, 2013.
[29] T.S. Wang, A.F. Hernandez, and G.M. Felker, et al. "Valvular heart disease in patients supported with left ventricular assist devices", Circ Heart Fail., vol.7, no.1, pp.215-22, 2014.
[30] M.S. Slaughter, F.D. Pagani, and J.G. Rogers, et al., " management of continuous-flow left ventricular assist devices in advanced heart failure", J Heart Lung Transplant., vol.29. no.4, Suppl.S1-39, 2010.
[31] P. Naiyanetr, F. Moscato, and M. Vollkron, et al., "Continuous assessment of cardiac function during rotary blood pump support: A contractility index derived from pump flow", J Heart Lung Transplant., vol.29, no.1, pp.37–44, 2010.

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