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Achieving flight with biohybrids

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Abstract

Biological muscles offer many functional advantages over mechanical systems in terms of energy efficiency, scalability, adaptiveness, self-generative capability and power-to-weight ratio. As such, biohybrid robots actuated by muscle tissues are attracting attention as promising candidates for the development of next-generation robots that can recapitulate the grace and fluidity observed in animal motion. Significant progress has been made in the fabrication of autonomous biohybrid robots capable of various forms of actuation and locomotion such as crawling, pumping and swimming. However, a major frontier that remains unexplored is flight in biohybrid locomotion. We envision that the development of flight would grant biohybrid greater accessibility to areas unreachable by land and sea, thus broadening its applicability. As a step towards this goal, we propose fabricating a biohybrid prototype capable of mimicking flight motion as seen in insects by capitalizing on the lessons learnt from previous studies. Instability of biological structures, short lifespan, slow muscular actuation, low energy output and mass optimization have been identified as the main challenges that will emerge over the course of this preliminary report. Herein, we propose adapting flight models used in synthetic insect robots and employing skeletal muscles in an antagonistic pair system for wing actuation. Our proposed study would pioneer the exploration of flight as a feasible locomotion in biohybrids and pave the way for the development of intelligent and autonomous biohybrid robots capable of flight, with potentially broad impact in robotics, bioengineering and aerodynamics.

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1. Introduction

As human technologies take on more of the characteristics of nature,
nature becomes a more useful teacher [1].

Over the past decades, robotic technologies have undergone rapid development to address the ever-expanding requirements of society. The emergence of bio-inspired robotics to emulate the performance of animals represents an exciting platform to develop dynamic solutions that can tackle real-world problems. Currently, many bio-inspired robots such as Snakebot [2] have been successfully fabricated with motors and electromechanical actuators. However, fine-actuation and energy remain as major bottlenecks with these mechatronic systems still lacking flexibility, energy efficiency, adaptiveness and power-to-weight ratio observed in musculoskeletal systems [3]. (A detailed comparison of biological tissues and mechatronic system is presented in **Table 1,** [4-11].) As such robots which can use biological muscles as actuators represent a promising approach to bridge this performance gap between animals and robots. This class of robots are known as biohybrid robots or simply, as bio-actuators since these devices are actuated by biological muscles.

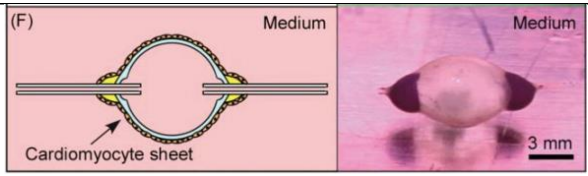
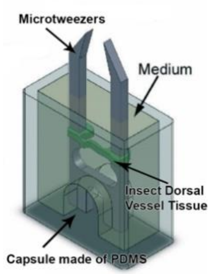
1.1 Overview of Biohybrid Prototypes

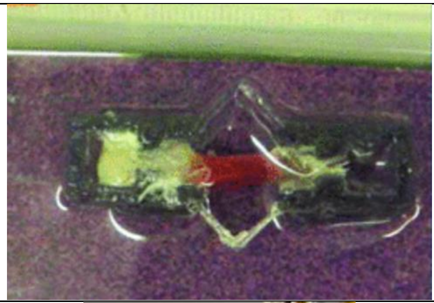
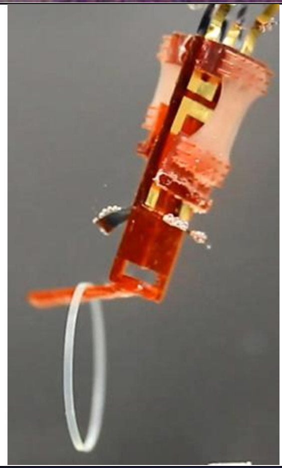
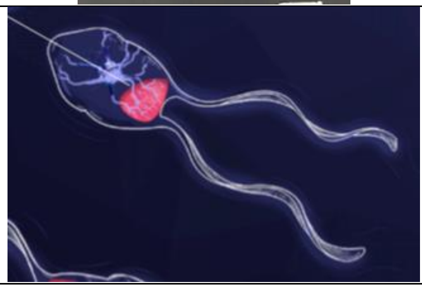
Biohybrid robots based on the integration of living muscles and soft materials into robotic systems, combines desirable attributes of muscles (**Table 1**) with those of artificial robots (high controllability [12] and artificial modifiability). Significant progress has been made in this area over the past decade with the fabrication of autonomous biohybrid robots capable of swimming, walking, grasping and pumping. **(Table 2).**

Table 1: Comparison of biological and mechatronics systems

	Biological Systems	Mechatronic systems
Energy and Power	Biological tissues have higher energy efficiencies (≥ 50%) [5] and higher power-to-weight ratio [6]. Furthermore, muscle tissues operate silently, utilize inexpensive and green fuel sources (e.g. simple sugars and fatty acids).	Traditional electromechanical systems have large heat losses with low energy transformation efficiency (<30%) [4].
Modulation of Force for Fine Actuation	Animal motion is driven by the coordinated movements of individual muscle cells with intrinsic molecular machinery to regulate contraction. By varying the number of myofibers recruited, they can efficiently modulate their stiffness, a property that is highly relevant in robotic	Although variable stiffness actuators can be produced in electric motors using a mechanical impedance and damping systems [7], the biological system offers a comparatively elegant and compact solution since it harnesses an inherent property of muscles.
Adaptiveness	• Adaptative strength through exercise [8]. • Healing after mechanical damage [9]. When damaged, a bio-actuator has the potential to self-regenerate in a few hours/days, recovering to its original performance • Intrinsic ability to sense and respond	• Self-healing only observed in external material and not in actuator/motor [10]. • Property limited to systems using soft materials
Scalability	Since muscles are modular, they confer biohybrid systems with high miniaturization ability which broadens their applicability.	Most traditional actuators such as electromagnetic motors cannot be scaled down without compromising on performance. Piezoelectric motors can be miniaturized, but they need (as do all artificial motors) to be powered by batteries, which cannot be efficiently scaled down in size at present [11].

Table 2: Overview of present biohybrids

S/N	Date	Description	Structure	Biomaterials	Non-living materials	Performance parameter	Control method	Ref
1	2006	Pumping		Cardiomyocytes	PDMS	Flow rate: 0.047 µL/min	No Control	[13]
2	2013	Manipulator		DV tissue	PDMS	Deflection: 250 µm Working 5 days	No Control	[14]
3	2016	Swimmer		Optogenetics cardiomyocytes	Sylgard 184, Sylgard 527, gold nanoparticles	Speed: 3.2 $mm \cdot s^{-1}$ Distance: 250 m	Optical control	[15]
4	2016	Crawler		I2 muscle from the buccal mass of *Aplysia californica*	Photocurable resin, collagen isolated from the *Aplysia* skin	Speed: 4.3 $mm \cdot min^{-1}$ Force: 58.5 mN	Electric Control	[16]

5	2017	Crawler		Neuromuscular tissue circuits from *Aplysia californica*	Photocurable resin	Speed: 0.54 $cm \cdot min^{-1}$	Electric and nervous system (chemical) control	[8]
6	2019	Grasping		Skeletal Muscle	Photoreactive acrylate resin, parylene, hydrogel and PDMS	Actuation angle: 90º of rotation around joint Lifespan: 1 week	Electrical Control	[17]
7	2019	Swimmer		Neutrosphere consisting of optogenetic skeletal muscle cells	PDMS	Speed: ~0.7 μm/s	Optical Control	[18]

PDMS: dimethylpolysiloxane; DV: dorsal vessels.

2. Background: An overview of the development of biohybrid robots

In this section, we will first identify and characterise relevant biological and artificial materials used in biohybrid literature. We will then review the commonly used control methods. Lastly, we will discuss macrostructural designs of current prototypes.

2.1 Biological Materials

Muscles are responsible for carrying main functions in biohybrids such as sensing and actuation. Biohybrid devices can use either tissues cultured from stem cells or whole muscle tissues excised from animals. While the use of explanted whole-muscle tissue provides a faster and more convenient method of obtaining biological materials, tissues cultured from cells offer more versatility owing to higher dimension controllability and longer lifespan [17]. Various types of muscles have been explored as potential bio-actuators, they are mainly cardiomyocytes, skeletal muscle cells, insect dorsal ventral tissue (DVT).

2.1.1 Cardiac Muscle Cells

Primary cardiomyocytes obtained from rats have been widely used as they are versatile and can generate large forces which allow them to actuate deformable structures. A swimming biohybrid had been successfully fabricated (**Table 2, S/N: 3**) by patterning cardiomyocytes onto a four-layer elastomeric structure. Upon contraction, the layer of cardiomyocytes bends the elastomeric structure together with the gold skeleton embedded within [15]. However, the applicability of cardiomyocytes is limited by their self-contractile nature, which means they cannot be 'switched on or off'.

2.1.2 Skeletal Muscle Cells

As the primary actuator system in mammals, skeletal muscles can operate over a wide range of lengths, forces and frequencies, making them an attractive option for biohybrid application. Biohybrid actuator resembling a human finger was developed by *Morimoto et al* using 3D skeletal muscle tissues cultured from myoblast-laden hydrogel sheet [17]. The actuator successfully performed pick-and-place manipulations. Unlike cardiac cells, skeletal muscle does not contract spontaneously, thus offers higher controllability. Furthermore, they can regenerate fibres in vitro after damage [19] while cardiomyocytes cannot, making them the superior candidate for development of biohybrids capable for self-healing.

2.1.3 Insect Tissue

Using insect dorsal vessel tissues (DVTs) instead of mammalian ones has the potential to develop extremely robust bioactuators as their cells have evolved to tolerate temperature and pH fluctuations since insects are incapable of thermal regulation [20]. At present, only insect-based systems can be kept alive and operative for months (up to 90 days) [21]. However, the low controllability of insect cells remains a major disadvantage of DVT-based devices as DVTs contracts spontaneously.

2.1.4 Other Invertebrate Tissues and Animals

Invertebrates living in extreme environments have unique properties that can be exploited, thus explored as novel sources of biohybrid material. For example, a crawling biohybrid was recently fabricated from sea slug muscles and collagen(**Table 2, S/N: 4**) [16] as sea slugs can withstand high osmotic pressures and substantial changes in temperature.

2.2 Material Selection

Standard robots utilize stiff materials (e.g. metals or hard plastics) and are inflexible[22]. To mimic the versatility of natural organisms, biohybrids require materials that are able to withstand movement-induced stress. Such materials include viscoelastic materials which exhibits both elastic and viscous behavior when deformed allowing for the dissipation of energy and maintenance of stability during motion [22] (e.g. muscles and PDMS) and soft materials which show high fracture toughness (e.g. hydrogels) which helps biohybrids achieve motion similar to actuation [22].

Another common issue with bioactuators is that they are confined to conducive aqueous environments [14]. Not only do the cells require nutrients such as glucose to convert into energy, drying of muscle tissues causes damage to biological components [14]. To combat this, Akiyama et al. [14] designed a capsule in which the medium is packaged together with DVTs (**Figure 1**).

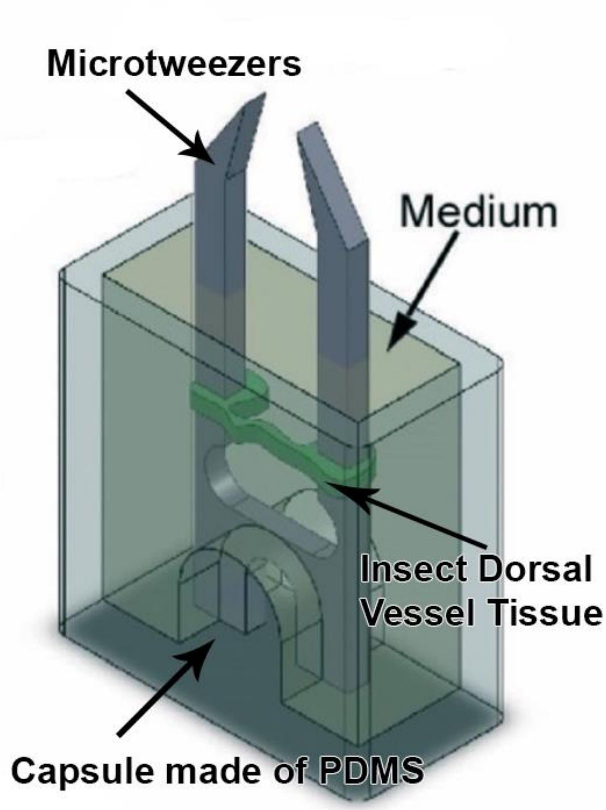


Figure 1: Micro-tweezers being packaged in medium, in a capsule made of PDMS, submerging the Insect DVTs. The gap between the capsule and the medium is filled with parylene materials which prevents the medium from evaporating [14].

2.3 Control

Controllability is a key determinant of biohybrid performance as it provides a way of coordinating muscle tissues to achieve actuation or locomotion. **Table 2** shows a wide range of control mechanisms employed in current biohybrids, including electrical, chemical and optogenetic stimulation.

2.3.1 Electrical Stimulation

Electrical stimulation is the most straightforward way of controlling muscles by directly stimulating the muscle tissues via electrical current using electrodes. By varying voltage and frequency, different types of motion can be achived. The muscles twitch at low frequencies, but assume a tetanus-like state at higher frequencies [17]. Examples of biohybrids that utilize this control method can be found in **Table 2 (S/N: 4 - 6)**. One caveat to this method is that bubbles generated by electrolysis at the electrodes causes degradation of muscle tissues and electrodes [17].

2.3.2 Chemical Stimulation

Alternatively, biohybrids can be controlled through chemical stimulation. The magnitude and frequency of muscle contraction can be regulated by using various chemicals [6]. An example of biohybrids that utilize this control method can be found in **Table 2 (S/N: 5)**. Naturally, chemical methods to control the biohybrid will be prone to diffusion. As such, if the muscle tissues are located are located spatially far away from the chemical source, the control effect will be weakened [6].

2.3.1 Optical Stimulation

Lastly, optical stimulation is increasingly popular for biohybrids by using optogenetically engineered myocytes which express light-sensitive ion channels. Light can then be used to selectively control the contraction of the muscle tissues [6]. Some examples of these biohybrids that utilize this control method can be found in **Table 2 (S/N: 3 & 7)**. However, prolonged exposure to light damages the biological components of the biohybrids, factors such as heat and radioactive effects on DNA and proteins must be considered. To solve this issue, limiting the duration of optical stimulation can be done [6]. Moreover, the layers surrounding the tissues to be controlled must be transparent for optical stimulation [6].

Biohybrids need to be as energy-efficient as possible and by employing the most effective control methods, efficiency can be maximized. However, efficiency of the biohybrid does not only stem from the materials and control methods alone: creative macro-structures also contribute to it.

2.4 Macrostructures

Creative macro-designs for biohybrids help to reduce the complexity of the robot or improve functionality of the biohybrid [22]. Creative macro-designs are designs that utilize the innate properties of materials to overcome shortcomings while reducing the number of moving parts or materials used in a design. By combining myocytes and mechanical properties, a wide range of motion can be achieved and to solve the shortcomings of biohybrids. One such problem is the spontaneous shrinkage of skeletal muscles which deforms and affects the muscle structure and function [17]. From observing natural biological systems, spontaneous shrinkage of muscle tissues rarely occur due to the existence of antagonistic pairs of skeletal muscles (a pair of connected muscles which selectively contracts and thus balances the total tension of the system between them) [17]. A way to combat this in the biohybrid system is to adapt from nature and use this system (**Figure 2**). This prevents the spontaneous shrinkage of muscle tissues. By doing this, this allows for a longer lifespan of a week [17].

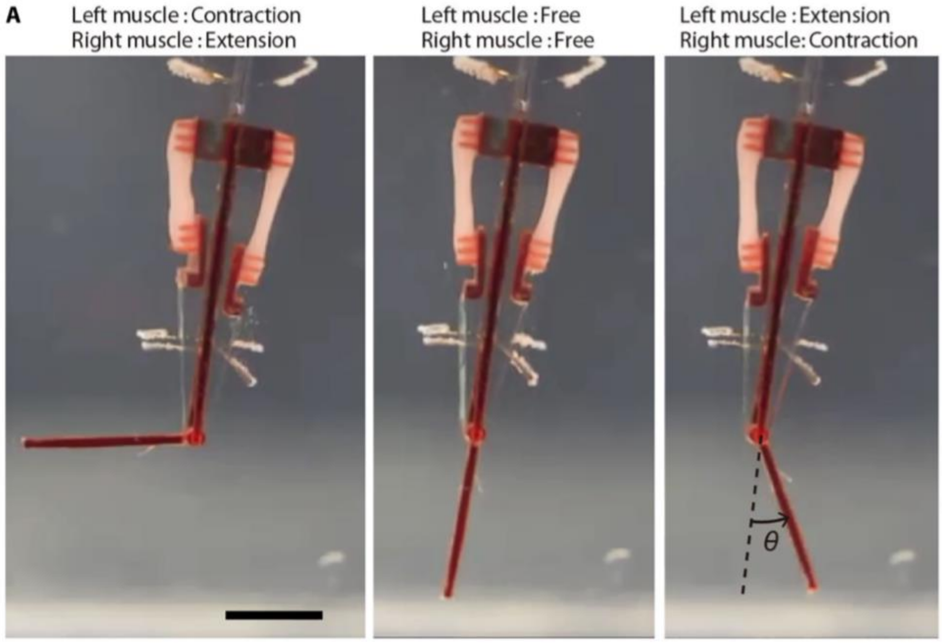


Figure 2: Antagonistic muscle pair system achieving bidirectional motion by choice of muscular contraction [17].

3. Research problem and Significance

Despite being in its nascent stage, biohybrids have the potential to become a new generation of robots that are multifunctional, power-efficient, intelligent and autonomous in ways similar to animals. This makes them suitable for navigation in extreme environment that are not only uncharted but also hostile. However, this task has been out of reach due to the lack of mature and stable prototypes. As mentioned previously, current biohybrid prototypes are restricted to only terrestrial and subaquatic motion (**Table 1**). We envision that the development of flying biohybrids will push the limits on biohybrid applicability. Behaving like drones, the use of flying biohybrids expands beyond exploration and search-and-rescue operations and into our daily lives for simple and mundane tasks like delivery. Unlike drones, flying biohybrids will be able to adapt and recover from damage, while being eco-compatible and inexpensive.

One exciting concept emerging in the field of robotics is of robotic swarms in which simpler and less sophisticated modular units work in teams to complete complex task. This concept draws inspiration from groups of insects that can perform tasks beyond the capabilities of individuals. *Science Robotics* predicts these swarms have the potential to solve the most pressing problems faced by human civilisation [3]. Flying biohybrids represents a potential candidate for such a concept as biohybrids are light (high power-to-weight ratio) and can be scaled down without compromising on performance.

As a step towards this goal, we propose fabricating a biohybrid prototype capable of mimicking flight motion observed in insects. This would result exploration of novel uses of materials and fabrication strategies. We believe that this preliminary study will pave the way for future cooperative studies between biomechanics, material engineering and aerodynamics by highlighting individual unexplored fields and discourse. Holistic approaches to efficiency, which must be eventually addressed for flight due to its high energetic cost [23, 24], will also benefit biohybrids of other forms.

4. Research Gaps

While significant progress has been made in many aspects of biohybrids such as materials and control strategies, none were specific to the context of flight. This section serves to identify the challenges that would surface in the process of mimicking flight motion of insects.

4.1 Rapid and reactive control

As previously stated, electrically stimulating skeletal muscles in antagonistic pairs twitch at low frequencies (1 Hz), but assume a tetanus-like state at higher frequencies (over 6.25 Hz) [17]. This is a cause of concern as muscles would be required to contract at high frequencies in order to achieve flight. Despite this immediate problem, further testing will need to be conducted in vitro within aerodynamic chambers to understand and maximize flight capabilities of low frequency oscillatory motion., such as gliding or hovering.

4.2 Energy output

Heavier-than-air flight is energetically expensive [23, 24]. Combating this is an easy recipe for falling in a vicious cycle: To improve flight capabilities, one must supply more energy. However, the increased onboard energy supply will result in greater weight, necessitating even more energy-demanding flight capabilities. Thus, ways to improve performance and efficiency via other means such as resonance and metabolic throughput needs to be investigated. To minimize energy wastage, unnecessary wing acceleration must be avoided. Energy should instead be stored and released for a subsequent wing stroke. This periodic energy input allows the use of inertia to maximize power output.

4.3 Longevity

Currently, biohybrid systems stimulated with electrodes pose a problem: bubbles that are generated by electrolysis cause degradation of the skeletal muscle tissues and electrodes [17]. A solution proposed by Morimoto et. al. was to use genetically engineered muscle cells that respond to optical stimuli [17]. However, this is not feasible as continuous optical stimulation of cells may damage the tissues as previously mentioned. A feasible control method for muscle tissues to maximize their longevity for bioactuation needs to be investigated.

Since biohybrid systems require a glucose-rich environment to function, the amount of glucose in the system will eventually be depleted: unlike from existing literature, continuous replacement of the medium in a flying biohybrid may not be feasible. The most straightforward option to this problem is to incorporate the regeneration of glucose in the medium, which needs to be addressed while fabricating flying biohybrids.

4.4 Mass optimization

As previously mentioned, soft materials such as PDMS, Hydrogels and various muscle cell types are used in fabricating a biohybrid. However, stiff materials are also needed for the frame of the biohybrid. For it to achieve flight, the mass of the entire biohybrid needs to be considered, this includes the frame and materials interacting with muscle tissues.

5. Future Directions

In understanding small scale oscillatory motion, we may be able to build a volant, or flying, biohybrid in the future, greatly enhancing the traversal ability of biohybrids. Furthermore, volant biohybrids provide a compelling alternative to mechanical drones for surveillance and delivery as mentioned above.

Immediate benefits to our study will be the ability to propose or construct a biohybrid that emulates insects better than existing technology, perhaps even outperforming them. Another key benefit is the study of achieving liberation from the nutrient-rich atmosphere, thereby expanding their practicality into open use. Furthermore, abstracting their operational reliance on other variables such as aerobic environments, gravitational field strength and clear runways can make biohybrids a viable option for hostile or extra-terrestrial exploration [25]. To achieve this, we put forth our proposal to study oscillatory motion by creating a functional model for testing using the lessons learnt from previous literature.

We propose to employ skeletal muscles in an antagonistic pair system for wing actuation **(Figure 3)**, as it will prevent spontaneous muscle shrinkage. Additionally, we will firstly explore the viability of a singular muscle pair to achieve flight. Higher complexity such as more muscle systems will be included for consideration if it is insufficient for flight.

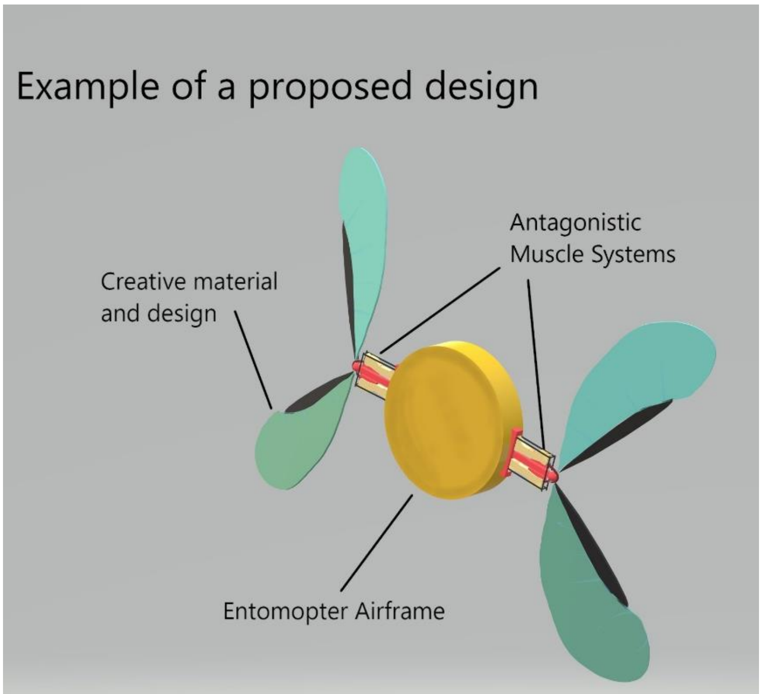


Figure 3: Graphic design of an example of structure that may be prototyped for purposes of this study.

With regards to flight, we plan to adapt synthetic insect flight models and designs, as there is a current lack of aerodynamic models employed by current biohybrid systems. Insect flight models and designs are the most applicable as they have similar physical scales to biohybrids, allowing them to behave as similarly as possible. This is due to the fluid behaviour the body is expected to experience being related to physical size. Thus, we propose using entomopters, which are micro-air vehicles (MAVs) that fly using the wing-flapping dynamics of insects (**Figure 5**). Designed to be energy efficient, Entomopters provide benefits over other airframes by being more discrete, inexpensive and non-reliant on runways [25, 26]. By capitalizing on mechanical resonance and well-integrated structures, Entomopters are capable of steerable flight [24, 25]. Innovative mechanical methods are also employed, such as this case in which the design stores and pressurizes waste gas products of the chemical muscle for ejection as an additional layer of flight and reaction control (**Figure 4**). Documented entomopters all capitalize on resonance, efficiently using limited energy capacity [25].

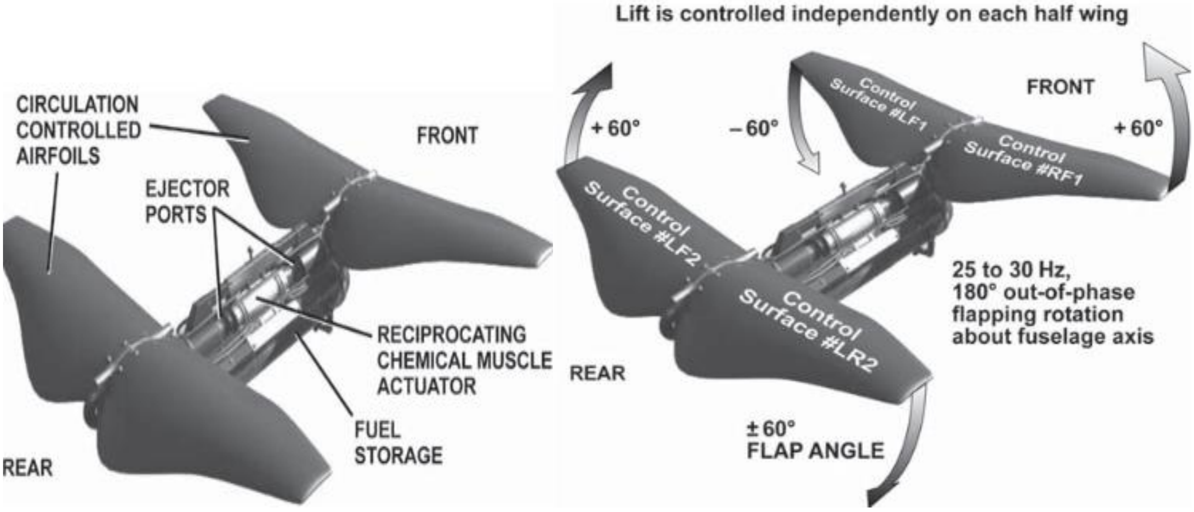


Figure 4: Schematic of the proposed design by Michelson [25]. The antiphase flapping and non-fixed wing stroke resemble insect flight mechanisms, allowing for motion in 3 degrees of freedom.

Coating hydrogel sheets in myoblasts can serve as skeletal muscle tissues, using a similar existing design [17], except replacing the joint with our wings to actuate them. Our main body can be made from. Additionally, flexible materials can be adapted to assist in energy efficiency and achieve resonance. Summing these ideas together will provide a foundation to build upon for studying oscillatory wing motion, and eventually flight, in biohybrids. We present an envisioned design in **Figure 3**.

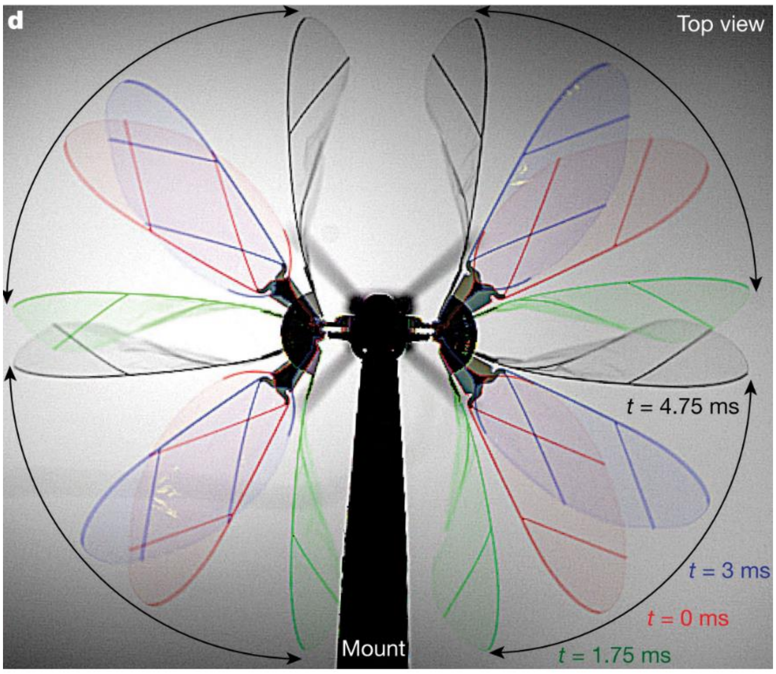


Figure 5: Example of an entomopter, the RoboBee also employs 2 sets of wings. This provides a small physical profile [24].

6. Conclusion

In summary, our project aims to adapt and employ well-studied methods and techniques in growing biohybrids to synthesize a proof of concept for oscillatory wing motion in small structures powered via biological means. This culminates into a primer for future endeavors into biological flight engines, with potential applications in surveillance, swarm technology and exploration.

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