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Multi objective optimization and experimental investigation of the stirring performance of a novel micro actuator

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Fragmented thrombolytic micro-actuators, a novel vascular recanalization technology, demonstrate potential excellent stirring performance in narrow and curved blood vessels. Optimizing their structural parameters and conducting performance evaluations are key areas of research in this field. This study employs the finite element (FE) method to numerically investigate the effect of critical structural parameters on the stirring performance of a novel scissor-type thrombolytic micro-actuator. A quadratic predictive model for its tip amplitude and stirring force is established using the Response Surface Methodology (RSM). Subsequently, the Non-dominated Sorting Genetic Algorithm III (NSGA-III) is utilized for Multi-Objective Optimization to identify the optimal combination of structural parameters. A micro-actuator prototype is fabricated and experiments on its stirring performance are conducted. The results indicate that the slit beam thickness has the most significant effect on stirring performance. After optimization, the maximum tip amplitude and maximum stirring force of the micro-actuator improve by 61.33% and 80.19%, respectively. This research lays a solid foundation for the miniaturization and clinical application of fragmented thrombolytic micro-actuators.

Keywords Micro-actuator, Multi objective optimization, Response surface methodology, NSGA-III, Fragmented thrombolysis

Abbreviations

RSM	Response surface methodology
NSGA	Non-dominated sorting genetic algorithm
NSGA-II	Non-dominated sorting genetic algorithm II
NSGA-III	Non-dominated sorting genetic algorithm III
RSM-NAGA-II	Response surface methodology non-dominated sorting genetic algorithm II
RSM-NAGA-III	Response surface methodology non-dominated sorting genetic algorithm III
MOO	Multi-objective optimization
MOPSO	Multi-objective particle swarm optimization
MOAHA	Multi-objective artificial hummingbird algorithm
BBD	Box–Behnken design
FE	Finite element
ANOVA	Analysis of variance
CCD	Central composite design
P-wave	Pressure wave
S-wave	Share wave

Ischemic stroke is primarily caused by arterial or venous embolism and has emerged as one of the leading causes of death worldwide in recent years^{1,2}. Current treatment methods commonly include pharmacological thrombolysis and mechanical thrombectomy^{3–5}. Compared to injected thrombolytic drugs, self-expanding stent retrievers, e.g., Merci Retriever and Solitaire Flow Restoration, can extend the treatment window by approximately 80%^{6–8}. In contrast to thrombectomy devices, fragmented thrombolytic micro-actuators precisely inject a small amount of thrombolytic medication at the site of the vascular lesion. Subsequently, they fragment

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and stir the thrombus to accelerate thrombolysis. This approach effectively reduces the risk of vascular injury associated with the retrieval of self-expanding stents while lowering the incidence of hemorrhage caused by high doses of thrombolytic agents. In addition, micro-actuators can be designed to be smaller and thus suitable for narrower blood vessels. Nonetheless, the lumen narrowing and curvature of the cardiovascular system create spatial limitations that significantly affect the stirring performance of micro-actuators. Therefore, there is an urgent need for structural parameter optimization and performance testing of fragmented thrombolytic micro-actuators, which highlights the critical importance of this research.

In general, transducers play a vital role in medical applications. Their high-frequency vibration characteristics allow them to effectively fragment diseased tissues, facilitating their removal and promoting healing⁹. For instance, Ajoudanian et al.^{10,11} employed the vibration mode transformation theory to design a slender micro-actuator with an end groove. In their device, the transducer generates longitudinal waves that transform into shear waves upon impacting the inclined surface of the groove, producing bending vibrations exclusively at the tip. This effectively disrupts blood clots while preserving vascular wall integrity. However, this actuator requires a specific length ratio between the beam and the slit beam (Fig. 1) to excite the ideal vibration mode¹¹. Based on the above work, Yang et al.¹² developed a novel scissor-type micro-actuator featuring an asymmetrical groove at the tip. This design enables the device to generate scissor-like bending vibrations, reducing the overall length of the actuator while meeting the stirring performance requirements.

Achieving maximum efficiency in converting longitudinal elastic waves generated by the transducer into transverse vibrations at the device tip within curved and narrow blood vessels poses a significant challenge, since transverse vibration is the most effective motion for dissolving thrombi. Appropriate optimization methods can effectively enhance the energy transfer efficiency of fragmented thrombolytic micro-actuators within a safe voltage range, thereby minimizing potential health risks to the patient. In another study, Yang et al.¹³ employed the finite element (FE) method to conduct a single-factor analysis of the micro-actuator structural parameters, using the tip amplitude as the response indicator. They revealed that changes in parameters such as the beam cross-sectional area, tip length and groove angle can significantly affect the tip response; hence, studying the sensitivity of a certain factor and the interactions between these factors is essential for achieving optimal tip response. Sensitivity analysis assesses the sensitivity of response outcomes to variables, enabling the identification of those variables that significantly affect these outcomes, enhancing the reliability of optimization models¹⁴. Ding et al.¹⁵ analyzed the effects of various structural parameters on the constant-force ratio factor and maximum deformation during the optimization of a typical flexure-based constant force module. They revealed that the bi-stable beam had the strongest effect on both objective parameters. Yu et al.¹⁶ employed Sobol sensitivity analysis in the lightweight design of the hydraulic power unit of a legged robot. They found that the motor diameter was the parameter with the most significant effect on the weight of the hydraulic power unit. The Response Surface Methodology (RSM), which is based on statistical and mathematical techniques, not only effectively reduces the number of experiments but also allows for a detailed examination of interactions among variables¹⁷. Furthermore, analysis of variance (ANOVA) can statistically identify the most suitable solutions for each model¹⁸. For example, Yang et al.¹⁹ developed an RSM optimization model for the thermal performance of a novel vortex generator, which improved the heat transfer capability by 19%. Kim et al.²⁰ applied RSM to optimize the design of composite wings for a tilt-rotor aircraft, finding that the rotor flutter speed increased from 13 to 18%.

Quadratic RSM can quickly identify interactions among variables during the structural optimization process. On this basis, Multi-Objective Optimization (MOO) algorithms can be utilized to balance multiple criteria.

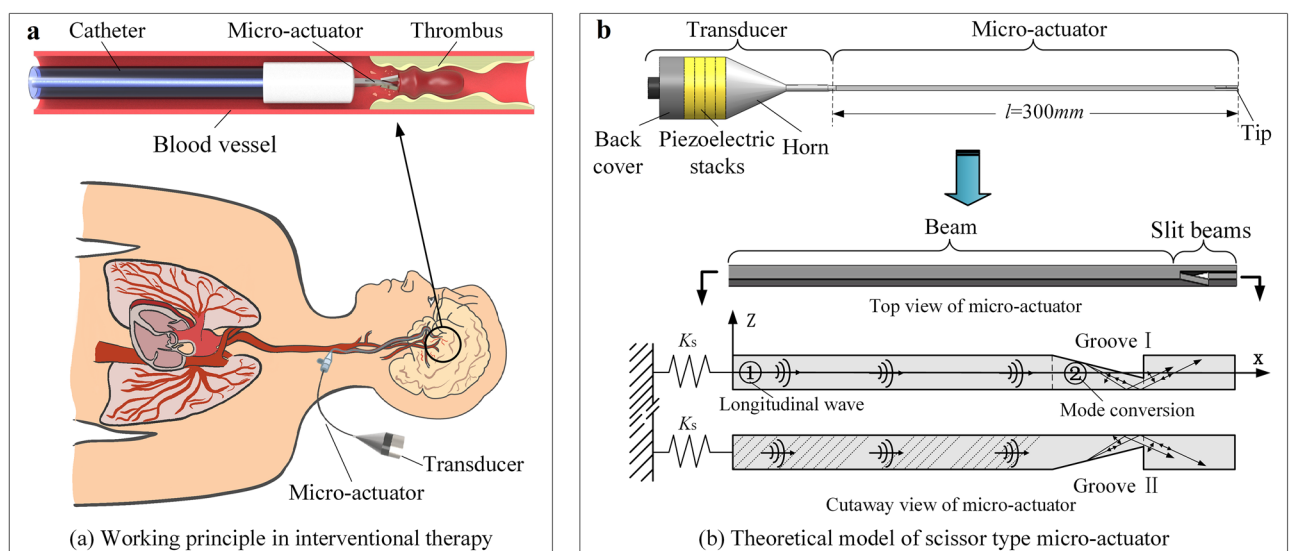


Fig. 1. Schematic diagram illustrating the (a) working principle in interventional therapy and (b) theoretical model of scissor type micro-actuator (created by Adobe Illustrator 2024, available at: <https://www.adobe.com/products/illustrator.html>).

Currently, MOO algorithms, such as the Non-dominated Sorting Genetic Algorithm (NSGA)^{21,22}, Multi-Objective Particle Swarm Optimization (MOPSO)²³, and Multi-Objective Artificial Hummingbird Algorithm (MOAHA)²⁴, are widely used to solve multi-objective structural optimization problems. Compared to other optimization algorithms, NSGA maintains population diversity while reducing computational complexity, rendering it a popular choice for engineering design. Barati et al.²⁵ employed the Non-dominated Sorting Genetic Algorithm II (NSGA-II) to perform MOO on transcatheter aortic valve stents. The optimization process reduced the maximum compressive strain by 40%, increased the radial strength by 261%, and decreased the eccentricity by 67%. Lv et al.²⁶ developed a Response Surface Methodology Non-dominated Sorting Genetic Algorithm II (RSM-NAGA-II) optimization model that improved the performance evaluation criteria of printed circuit heat exchangers by 8.5% and reduced entropy production by 9.98%. Zhu et al.²⁷ employed the Response Surface Methodology Non-dominated Sorting Genetic Algorithm III (RSM-NAGA-III) MOO method to assess the effect of geometric parameters of magnesium alloy ureteral stents on degradation performance. The optimized stents achieved a 5.52-fold improvement in degradation uniformity and a 10-fold extension in degradation time. Akbar et al.²⁸ reported that the Non-dominated Sorting Genetic Algorithm III (NSGA-III) provides more diverse alternatives than NSGA-II.

Based on the aforementioned literature review, this study first investigates the effect of different materials for the horn on the stirring performance of a fragmented thrombolytic micro-actuator. The reference angle for the asymmetric groove is determined according to Snell's law. Subsequently, factors affecting structural optimization are identified using a dynamic model of the fragmented thrombolytic micro-actuator, with the tip amplitude and stirring force serving as the stirring performance indicators, a higher value for both indicators indicates better stirring performance of the micro-actuator. Through single-factor FE experiments, a quadratic regression model for these indicators is fitted through RSM. Then, NSGA-II and NSGA-III are employed to perform MOO on the response functions of the micro-actuator to obtain the optimal structural parameters. Lastly, prototypes are manufactured based on the optimal parameters, which are used in experimental studies. To the best of the authors' knowledge, this study is the first to integrate the RSM and NSGA-III algorithms and apply MOO analysis to fragmented thrombolytic micro-actuators.

Methods

Micro-actuator principle and characteristics

Micro-actuator basic structure and working principle

Yang et al.¹² proposed a novel fragmented thrombolytic micro-actuator with asymmetric grooves at the tip of a cantilever beam. Building on their work, this study introduces a horn to the transducer section and modifies the piezoelectric vibrator into a cylindrical shape that adheres to the horn. In this way, the longitudinal energy generated by the transducer is efficiently transmitted to the tip of the device, producing scissor-like stirring vibrations. Based on the interventional length for treating carotid artery stenosis^{29,30}, the length l of the micro-actuator was set to 300 mm. A slit was cut along the centerline of the beam, separating the tip of the micro-actuator into two slit beams. Subsequently, two asymmetric grooves were cut at the tip of the slit beams as shown in Fig. 1. The pressure wave (P-wave) generated by the transducer propagates through the beam and impacts the inclined surfaces of the grooves. Due to wave reflection, the P-wave is converted into shear waves (S-waves) in the vertical direction. The grooves generate out-of-phase bending moments that cause the slit beams to bend in opposite directions. The deflections caused by the two opposing moments cancel each other out, enabling the device to maintain a horizontal position while producing an asymmetric deflection at its tip, resembling a scissor shape.

When the driving frequency of the transducer approaches the desired frequency, a scissor-like vibration mode is excited. Bending is concentrated at the tip, while other sections remain undisturbed. This effectively improves energy transmission efficiency and prevents contact damage caused by unnecessary bending. Considering that excessive driving voltage may harm patients and the small size of the fragmented thrombolytic micro-actuator results in small tip amplitude and stirring force, improving the vibration mode conversion efficiency becomes essential.

Transducer shape selection

The novel fragmented thrombolytic micro-actuator features a sandwich-type transducer at its front as shown in Fig. 2, which operates at different resonance frequencies corresponding to various vibration modes. The longitudinal vibration wave it generates is crucial for achieving optimal system performance. This transducer comprises a back cover plate, piezoelectric stacks, and a horn arranged longitudinally. The piezoelectric stack enables conversion between mechanical and electrical energy³¹. In this research, an alternating electric field is applied to the piezoelectric stack, leveraging the inverse piezoelectric effect to induce vibrations at a specific frequency in the piezoelectric material. The vibration waves are transmitted through the horn to the tip of the micro-actuator, generating stirring vibrations that disrupt thrombi. Notably, during thrombolysis, the micro-actuator can also convert mechanical energy into electrical energy through the piezoelectric layer. In this case, the piezoelectric layer acts as an energy harvester, powering implanted sensors or low-power circuits and reducing dependence on external power sources³².

The diameter of cerebral arteries is approximately 3.2 mm³³. To enhance energy transfer efficiency, the transducer tip diameter should be close to that of the cerebral artery. Given that the aim of this study is optimization, R_2 (end radius of horn) was selected as 1.9 mm to facilitate experimental observations and reduce costs. The standard size of the piezoelectric actuator was chosen as $\phi 38 \text{ mm} \times \phi 13 \text{ mm} \times 6.35 \text{ mm} \times 4$ (outer diameter $\times$ inner diameter $\times$ height $\times$ number); thus, R_1 (starting radius of the horn) = 19 mm.

The boundary conditions were set as follows³⁴:

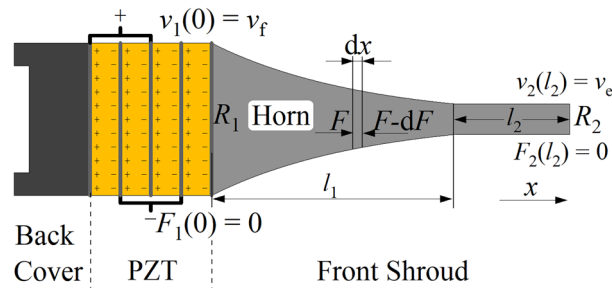


Fig. 2. Schematic diagram of the sandwich-type transducer.

$$\begin{cases} v_1(0) = v_f \\ F_1(0) = 0 \\ v_1(l_1) = v_2(0) \\ F_1(l_1) = F_2(0) \\ F_2(l_2) = 0 \\ v_2(l_2) = v_e \end{cases} \quad (1)$$

According to Hooke's law and Newton's second law, the increment of the elastic force on the dx microelement segment in Fig. 2 can be expressed as:

$$Y \frac{\partial}{\partial x} \left[S(x) \frac{\partial \xi}{\partial x} \right] dx = \rho S(x) dx \frac{\partial^2 \xi}{\partial t^2} \quad (2)$$

where $S(x)$ is the cross-sectional area at x on the axis, mm^2 ; Y is the Young's modulus, GPa; $\frac{\partial \xi}{\partial x}$ is the strain, and ρ is the material density, kg/m^3 .

Since the speed of sound in the device is $c = (Y/\rho)^{1/2}$, and the wave number is $k = \omega/c$, the device is in simple harmonic motion when³⁴:

$$\begin{cases} \xi = \xi e^{j\omega t} \\ v = j\omega \xi \end{cases} \quad (3)$$

The equation of motion for the horn is:

$$\frac{\partial^2 \nu}{\partial x^2} + \frac{1}{S(x)} \frac{\partial S(x)}{\partial x} \frac{\partial \nu}{\partial x} + k^2 \nu = 0 \quad (4)$$

When the transducer performs simple harmonic motion, the horn amplifies the longitudinal vibration wave generated by the transducer and transmits it to the micro-actuator tip, exciting vibrations at the tip. The shape and size of the horn directly affect the amplification factor M_p and the resonant frequency f of the transducer. The stepped horn experiences significant energy loss at its varying cross-sections, while the gradually tapered horn can minimize longitudinal energy loss. Therefore, this study analyzes the frequency equations and mathematical models for the amplification factors of three different tapered horn shapes, as summarized in Table 1³⁴.

The effect of geometry of the transducers l_1 and l_2 with different structures on their resonant frequency and velocity amplification in the longitudinal mode was analyzed, as shown in Figure 3.

When kl_1 was equal to 2, the amplification factors M_p of the conical and exponential transducers reached their maximums at 45.12 and 27.02, respectively. When kl_1 was equal to 2.3, the amplification factor M_p of the catenary transducer reached its maximum at 24.19. The amplification factor M_p of the conical transducer was higher, resulting in greater vibration energy transfer efficiency. Therefore, a conical transducer with a ratio of l_1 to l_2 equal to 2:1.387 was selected.

In general, if the frequency of the transducer is specified, its shape and dimensions can be determined via the frequency equation³⁵. To assess the effect of horn materials on actuator stirring performance, the following materials were selected for the horn: SUS304, SUS316, SUS316L, Al7075, and Al6061; their properties are listed in Table 2.

By substituting the above material properties into the frequency equation for a cylindrical horn, the relationship between the length l_1 and the natural frequency f can be established. The frequency corresponding to the scissor-like mode generated by the micro-actuator was 4250 Hz. The length l_1 values for different horn materials are presented in Figure 4.

For a conical transducer with a ratio of l_1 to l_2 of 2:1.387, the dimensions of horns made of different materials were calculated, as listed in Table 3.

Groove reference angle determination

The groove angle (Fig. 1) at the tip of the novel micro-actuator is equal to the incidence angle of the P-wave. The P-wave generated by the transducer propagates through the beam to reach the groove. Upon impacting the

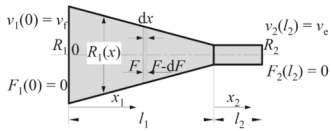
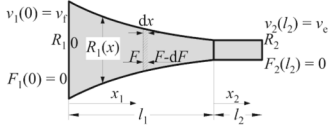
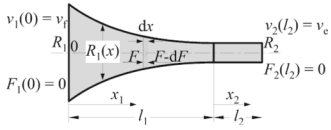
Horn shape	Frequency equation	Amplification factor expression
Conical horn: 	$\operatorname{tg} kl_2 = \{81kl_1 - [10(kl_1)^2 + 81] \operatorname{tg} kl_1\} \div [kl_1 (10kl_1 - 9\operatorname{tg} kl_1)]$	$\frac{v_e}{v_f} = \frac{10 \cos kl_1}{\cos kl_2} - \frac{90 \sin kl_1}{kl_1 \times \cos kl_2}$
Exponent horn: 	$\operatorname{tg} kl_2 = kl_1 / \left\{ \ln 10 - \sqrt{1 - \left(\frac{\ln 10}{kl_1} \right)^2} \right. \\ \left. \times kl_1 \operatorname{ctg} \left[kl_1 \sqrt{1 - \left(\frac{\ln 10}{kl_1} \right)^2} \right] \right\}$	$\frac{v_e}{v_f} = \left\{ 10 \sin \left[kl_1 \sqrt{1 - \left(\frac{\ln 10}{kl_1} \right)^2} \right] \right\} \div \sin kl_2 \sqrt{1 - \left(\frac{\ln 10}{kl_1} \right)^2}$
Hyperbolic cosine horn: 	$\operatorname{tg} kl_2 = \frac{1}{kl_1} \left\{ (\cosh^{-1} 0.1) \frac{3\sqrt{11}}{10} + kl_2 \sqrt{kl_1^2 - (\cosh^{-1} 10)^2} \right. \\ \left. \times \operatorname{tg} \left[\sqrt{kl_1^2 - (\cosh^{-1} 10)^2} \right] + \left\{ \frac{3\sqrt{11}(\cosh^{-1} 10)}{10kl_1 \sqrt{kl_1^2 - (\cosh^{-1} 10)^2}} \right\} \right. \\ \left. \times \operatorname{tg} \left[\sqrt{kl_1^2 - (\cosh^{-1} 0.1)^2} \right] - 1 \right\}$	$\frac{v_e}{v_f} = - \left\{ 30\sqrt{11} \cosh^{-1} 10 \right. \\ \left. \times \sin \left[\sqrt{kl_1^2 - (\cosh^{-1} 10)^2} \right] \right. \\ \left. + 10 \cos \left[\sqrt{kl_1^2 - (\cosh^{-1} 10)^2} \right] \right\} \div \left[\sqrt{kl_1^2 - (\cosh^{-1} 10)^2} \right] \times \cos kl_1$

Table 1. Frequency equations and amplification factors for different horns.

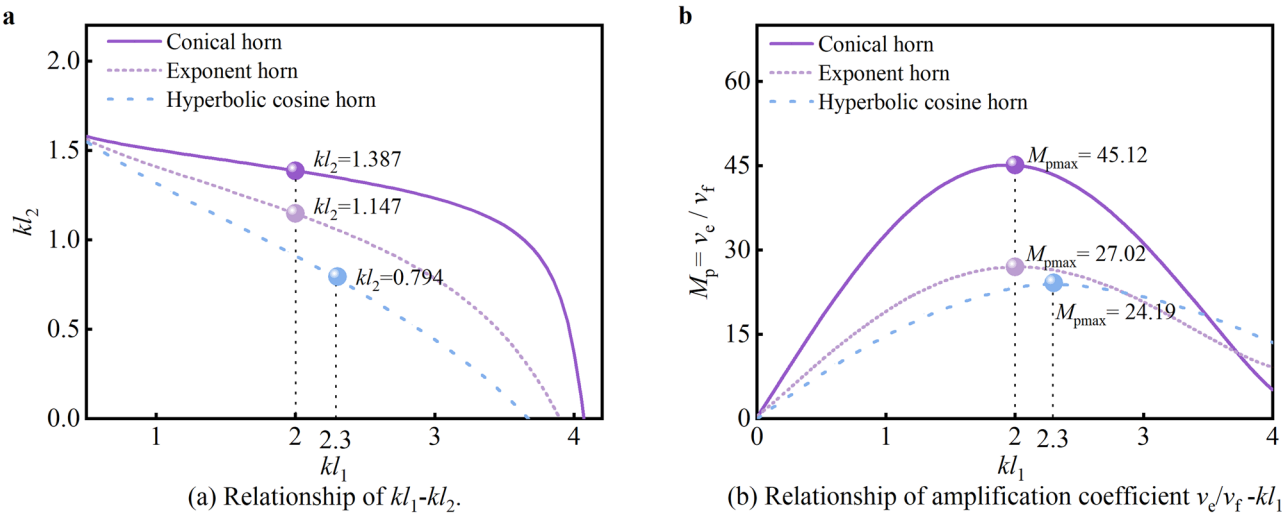


Fig. 3. Resonant frequency and amplification factor of the three transducers.

Material	Density ρ (kg/m ³)	Young's modulus E (GPa)	Poisson's ratio ν
SUS304	7930	195	0.29
SUS316	7980	193	0.28
SUS316L	8000	193	0.29
AL7075	2810	70	0.33
AL6061	2750	69	0.33

Table 2. Material properties of horns.

inclined interface of different media, P-waves convert into S-waves due to reflection at the interface, as illustrated in Fig. 5. This phenomenon facilitates the conversion of the longitudinal vibrations at the tip of the micro-actuator into transverse vibrations.

According to Snell's law³⁶, the equations for the reflection and mode conversion of a P-wave impacting at angle θ are as follow:

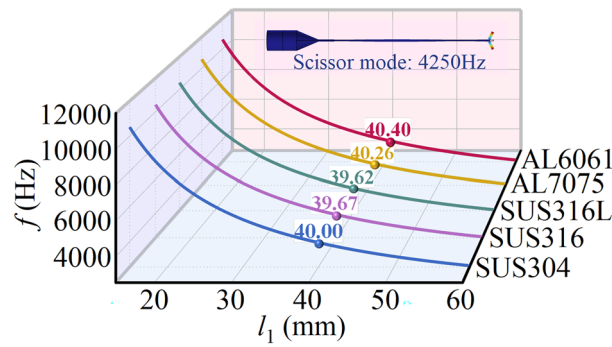


Fig. 4. Relationship $f-l_1$ of the transducer for different horn materials.

Material	l_1 (mm)	l_2 (mm)
SUS304	40.00	27.74
SUS316	39.67	27.51
SUS316L	39.62	27.47
AL7075	40.26	27.92
AL6061	40.40	28.02

Table 3. Dimensions of horns made of different materials.

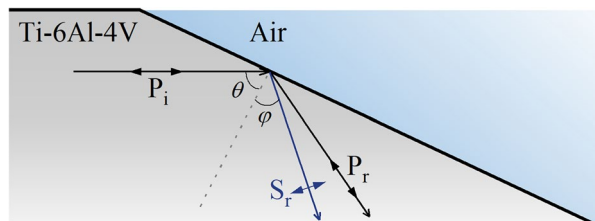


Fig. 5. Reflection and mode conversion of incident longitudinal waves impacting on the Ti-6Al-4V /air interface.

$$\frac{\nu_p}{\sin \theta} = \frac{\nu_s}{\sin \varphi} \quad (5)$$

$$R_{pl} = \left[\frac{\cos^2 2\varphi - (\nu_s/\nu_p)^2 \sin 2\theta \sin 2\varphi}{\cos^2 2\varphi + (\nu_s/\nu_p)^2 \sin 2\theta \sin 2\varphi} \right]^2 \quad (6)$$

$$R_{sl} = \frac{4(\nu_s/\nu_p)^2 \cos^2 2\varphi \sin 2\theta \sin 2\varphi}{[\cos^2 2\varphi + (\nu_s/\nu_p)^2 \sin 2\theta \sin 2\varphi]^2} \quad (7)$$

where ν_p is the velocity of the longitudinal wave, m/s; ν_s is the velocity of the transverse wave, m/s; which according to Ref.³⁷ are $\nu_p=5900$ m/s and $\nu_s=3016$ m/s for Ti-6Al-4V; R_{pl} and R_{sl} are the energy reflection coefficients of the longitudinal and transverse waves, respectively. Energy reflection coefficient versus angle of incidence, as illustrated in Fig. 6.

According to Fig. 6, at an incidence angle of 67° , the energy reflection coefficient of the transverse wave is maximized, with the energy conversion loss remaining below 3.5%. This is crucial for achieving high performance. Therefore, $\theta=67^\circ$ was chosen as the reference value for the groove angle at the tip. Moreover, an amount of energy passes through the inclined surface, causing interference with the reflected transverse wave. It is noteworthy that different types of grooves may affect the stirring performance of the micro-actuator tip³⁸. To this end, this study developed FE models with different incidence angles to determine the optimal value.

Micro-actuator mathematical model

The beam and tip of the micro-actuator operate in two distinct vibration modes. The dynamic model of the micro-actuator was simplified into longitudinal and transverse components³⁹, as illustrated in Fig. 7.

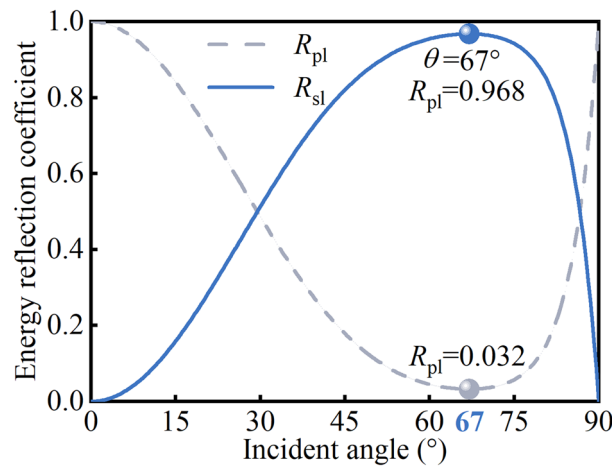


Fig. 6. Energy reflection coefficient versus angle of incidence θ .

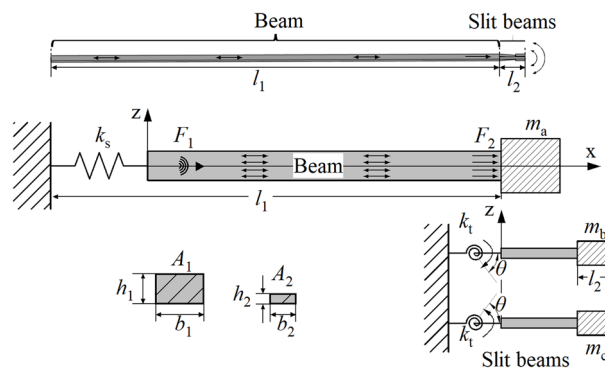


Fig. 7. Dynamic model of micro-actuator.

In this model, the left end of the beam is connected to a transducer providing longitudinal elastic force, which is described by a spring boundary (k_s). The actuator tip is replaced by a mass block attached to the right end of the beam. In the transverse vibration mode at the tip, the bending deflection is concentrated in the notch, which is modeled as a slit beam connected vertically to a torsion spring (k_t) to simulate the bending motion at the left end. At the same time, the tip is replaced by a mass block (m_b/m_c).

Assuming that the deformation of the beam and the slit beams occurs only in the x - z plane, the motion equation for the longitudinal vibration of the beam is:

$$[\rho A_1 + m_a \delta(x - l_1)] \frac{\partial^2 u}{\partial t^2} - EA_1 \left[\frac{\partial^2 u}{\partial x^2} \right] + c \frac{\partial^3 u}{\partial x^2 \partial t} = (F_1 \delta - ku)(x - 0) \quad (8)$$

The motion equation for the longitudinal vibration of the slit beams is:

$$[\rho A_2 + m_b \delta(x - l)] \frac{\partial^2 z}{\partial t^2} + \frac{\partial^2}{\partial x^2} \left[EI(1 + c \frac{\partial}{\partial t}) \frac{\partial^2 z}{\partial x^2} \right] = (\gamma F_2 \delta' - k\theta)(x - l_1) \quad (9)$$

where u is the longitudinal vibration displacement of the beam, mm; z is the transverse vibration displacement of the slit beam, mm; δ is the Dirac coefficient; F_1 is the input force of the transducer, N; ρ is the density of the beam, kg/m³; A_1 is the cross-sectional area of the beam, m²; A_2 is the cross-sectional area of the slit beam, m²; I is the moment of inertia, m⁴; E is the Young's modulus, Pa; γ is the force conversion factor; c is the damping coefficient.

Equations (8) and (9) indicate that the output amplitude at the micro-actuator tip primarily depends on material density ρ , input force F_1 , force conversion factor γ , beam cross-sectional area A_1 , slit beam cross-sectional area A_2 , and tip masses m_b and m_c . Since the input force F_1 can be adjusted by the input voltage, and the selected micro-actuator material is Ti-6Al-4V, the input force F_1 and the material density ρ were not analyzed. In addition, the force conversion factor γ depends mainly on the groove angle θ , the tip masses m_b and m_c are primarily affected by the tip length l_2 , and the cross-sectional area of the slit beam is related to its

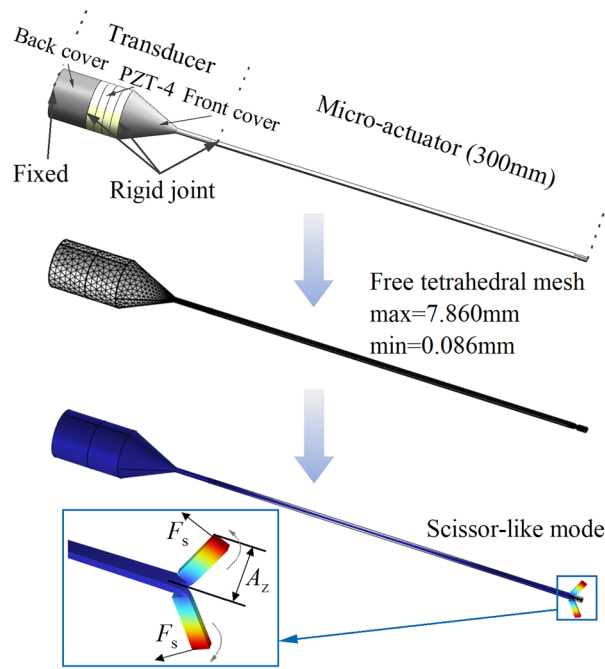


Fig. 8. FE model of the micro-actuator.

Material	Density ρ (kg/m ³)	Young's modulus E (GPa)	Poisson's ratio ν
Ti-6Al-4V	4510	110	0.32

Table 4. Micro-actuator material parameters.

thickness h_2 . Therefore, the structural parameter optimization of the micro-actuator should focus on analyzing the groove angle θ , beam cross-sectional area A_1 , slit beam thickness h_2 , and tip length l_2 .

Effect of structural parameter interaction on tip response characteristics

Fragmented thrombolytic micro-actuator FE analysis

The FE model of the fragmented thrombolytic micro-actuator is exhibited in Fig. 8. To ensure efficient fragmentation and dissolution of thrombi, the output vibration response at the tip of the micro-actuator must be maximized, while operating within the safe voltage range for the human body. To this end, a PZT-4 transducer with low dielectric loss was selected and subjected to 100V. Its front and back cover materials were set as SUS304. The micro-actuator is made of Ti-6Al-4V, which has good biocompatibility⁴⁰; its material parameters are listed in Table 4. The back cover was fixed as a constraint. The interface between the cover and the piezoelectric vibrator, as well as that between the micro-actuator and the transducer, were set as rigid connections. The remaining surfaces were set as free.

Due to the significant differences in the mechanical properties of thrombi at various locations, the micro-actuator should be able to generate different amplitudes and stirring forces based on the surgical requirements. Therefore, this study used the output amplitude at the tip and the stirring force as two indicators for evaluating the stirring performance of the micro-actuator. Accordingly, the Z-direction tip amplitude A_z and stirring force F_s were analyzed. The expression for the simple harmonic motion of the micro-actuator is as follows:

$$\begin{cases} A_z = A_{z_{\max}} \sin(2\pi f) \\ F_s = -4\pi^2 f^2 m A_{z_{\max}} \sin(2\pi f) \end{cases} \tag{10}$$

where f is the corresponding frequency of the scissor-like mode, Hz; $A_{z_{\max}}$ is the Z-direction tip amplitude, m; and F_s is the stirring force at the tip, N.

The FE model of the micro-actuator was meshed with 38,651 tetrahedral elements. In the model, the horn material was SUS304, the beam cross-sectional area was $A_1=6\text{ mm}^2$, the groove angle was $\theta=67^\circ$, the slit beam thickness was $h_2=0.4\text{ mm}$, and the tip length was $l_2=7\text{ mm}$. The mesh independence of the FE model was verified and the results are shown in Table 5. For the models with 15,244 and 25,835 elements, the relative deviation in the Z-direction amplitude $A_{z_{\max}}$ was 14.1%, and that in the stirring force $F_{s_{\max}}$ was 16.7%. For those with 25,835 and 38,651 elements, the relative deviation in $A_{z_{\max}}$ was 15.7% and in $F_{s_{\max}}$ was 16.9%. When the models with 38,651 and 89,909 elements were compared, the relative deviation in $A_{z_{\max}}$ was 0.8%,

Number of elements	Z-direction amplitude $A_{z_{\max}}$ (μm)	Stirring Force $F_{s_{\max}}$ (N)
15,244	27.44	0.78
25,835	23.56	0.65
38,651	19.86	0.54
65,832	19.80	0.54
89,909	19.69	0.53

Table 5. Mesh-independence verification results.

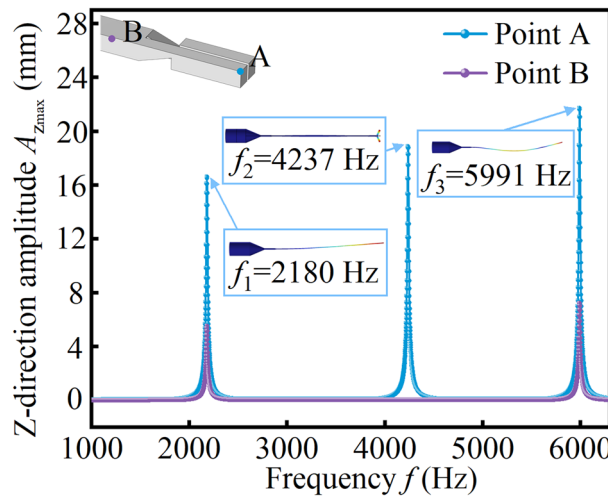


Fig. 9. Harmonic analysis of FE model.

and in $F_{s_{\max}}$ was 1.8%. Considering both computational speed and accuracy, the model with 38,651 elements was selected for FE analysis.

When the micro-actuator operates in the scissor-like mode, the two slit beams at the tip exhibit an anti-symmetric motion in the Z-direction, forming a scissor-like shape, while the other regions experience negligible displacement. This indicates that the scissor-like mode of the micro-actuator has been successfully excited.

To accurately predict the dynamic response of the micro-actuator, Rayleigh damping must be applied to the FE model. The expression for the Rayleigh damping matrix is as follows:

$$\begin{cases} = \alpha[M] + \beta[K] \\ \alpha = 4\pi f_n f_a \zeta / (f_n + f_a) \\ \beta = \zeta / (\pi f_n + \pi f_a) \end{cases} \quad (11)$$

where $[C]$ is the damping matrix; $[M]$ is the mass matrix; $[K]$ is the stiffness matrix; α and β are the scaling coefficients; ζ is the damping ratio with the value of 2%¹³; f_n denotes the frequency of the required vibration mode for the micro-actuator specifically corresponding to the scissor-like mode; f_a represents the frequency of vibration modes adjacent to the scissor-like mode.

Harmonic analysis of the micro-actuator FE model (Fig. 9) revealed that the scissor-like mode occurs at frequency f_2 , with $f_n = f_2 = 4237$ Hz. The adjacent vibration mode manifests at frequency f_1 , where $f_a = f_1 = 2180$ Hz. By substituting $f_n = f_2 = 4237$ Hz and $f_a = f_1 = 2180$ Hz into Eq. (11), the damping matrix of the FE model of the micro-actuator can be obtained.

The second resonance mode of the FE model corresponds to the scissor-like mode, which is crucial for this study. In this vibration mode, the micro-actuator generates displacement exclusively at the tip, while other areas remain undisturbed. This effectively prevents damage to blood vessel walls by avoiding bending vibrations in other regions of the micro-actuator and significantly reduces vibrational energy loss. Under the scissor-like mode, the opposing vibrations of the dual slit beams at the tip generate a greater amplitude compared to alternative modes, indicating enhanced thrombolytic efficiency in this configuration.

Given the superior stirring performance and safety characteristics of the scissor-like mode, subsequent analysis focuses on the output response of the fragmented thrombolytic micro-actuator in this mode, specifically evaluating the maximum amplitude $A_{z_{\max}}$ and stirring force $F_{s_{\max}}$.

Effect of material on tip vibration response

Horns with different material properties were tested, while the following parameters remained constant: beam cross-sectional area $A_1 = 6 \text{ mm}^2$ (with $b_1 = 3 \text{ mm}$ and $h_2 = 2 \text{ mm}$), groove angle $\theta = 67^\circ$, slit beam thickness $h_2 = 0.4$

mm, and tip length $l_2=7$ mm. Using time-domain analysis in the scissor-like mode, the effect of different horn materials on the tip response of the micro-actuator was explored, as shown in Fig. 10.

It can be observed that, when the was made of SUS304, the tip amplitude of the micro-actuator reach 19.86 μm . Therefore, this study selected SUS304 as the material for the transducer horn.

Effect of micro-actuator structural parameters on tip response

Figure 11a shows the effect of equal proportional variation of the beam cross-sectional area A_1 on the tip response of the micro-actuator when $\theta = 67^\circ$, $h_2 = 0.4$ mm, and $l_2 = 7$ mm. In the given parameter range, both the $A_{z_{\max}}$ and $F_{s_{\max}}$ of the micro-actuator tip exhibited a trend of increasing first and then decreasing, with the peak value appearing at $b_1 = 3$ mm and $h_1 = 2$ mm.

Figure 11b presents the effect of the groove angle θ on the tip response of the micro-actuator when $A_1 = 6$ mm² ($b_1 = 3$ mm, $h_1 = 2$ mm), $h_2 = 0.4$ mm, and $l_2 = 7$ mm. Analyzing the reference angle range of $67^\circ \pm 10^\circ$, both the A_z and F_s of the micro-actuator tip exhibited a trend of increasing first and then decreasing. By fitting the simulation value, the $A_{z_{\max}}$ and $F_{s_{\max}}$ values were found to be in the range of 65° – 67° , which was similar to the reference angle calculated by Snell's law.

Figure 11c demonstrates the effect of the slit beam thickness h_2 on the tip response of the micro-actuator when $A_1 = 6$ mm² ($b_1 = 3$ mm, $h_1 = 2$ mm), $\theta = 67^\circ$, and $l_2 = 7$ mm. For a given slit beam thickness h_2 in the range of 0.2 mm–0.6 mm, both the $A_{z_{\max}}$ and $F_{s_{\max}}$ at the tip of the micro-actuator exhibited a trend of increasing first and then decreasing. This is due to that, under high-frequency vibration, an excessively thin slit beam reduces energy transfer efficiency, allowing only a small portion of the longitudinal wave to be converted into a transverse wave at the groove and transmitted to the tip. On the other hand, an excessively thick slit beam enhances structural stiffness, hindering the effective excitation of the micro-actuator tip.

Figure 11d shows the effect of the tip length l_2 on the tip response of the micro-actuator when $A_1 = 6$ mm² ($b_1 = 3$ mm, $h_1 = 2$ mm), $\theta = 67^\circ$, and $h_2 = 0.4$ mm. For a given tip length l_2 in the range of 6 mm–10 mm, both the $A_{z_{\max}}$ and $F_{s_{\max}}$ of the micro-actuator tip exhibited a trend of increasing first and then decreasing. An excessively short tip limits its amplitude in the Z-direction, while an excessively long tip increases its weight, thereby limiting its amplitude.

Sensitivity analysis evaluates the effect of input parameters on the tip response of the micro-actuator, encompassing both local and global approaches. Local sensitivity analysis is suitable for linear output responses; however, it cannot capture nonlinear responses⁴¹. In contrast, global sensitivity analysis (e.g., the Sobol index method) quantifies the variance contribution of structural parameters across the entire input space, capturing both main effects and higher-order interactions in complex nonlinear systems⁴². As depicted in Fig. 11, significant nonlinear correlations exist between tip responses and structural parameters in the micro-actuator. Hence, building on the single-factor analysis results, this study employs the Sobol index method to assess parameter sensitivity.

The Sobol index is calculated as follows:

$$S_i = \frac{\text{Var}(Y|X_i)}{\text{Var}(Y)} \quad (12)$$

where S_i denotes the Sobol index of structural parameters, a higher value indicates greater sensitivity to the tip response of the micro-actuator. Moreover, $\text{Var}(Y|X_i)$ is the conditional variance of response Y under parameter X_i , $\text{Var}(Y)$ is the total variance of Y . S_A , S_θ , S_h , and S_l are the Sobol indices of the beam cross-sectional area, groove angle, slit beam thickness, and tip length, respectively. The Sobol indices for key structural parameters are summarized in Table 6.

Table 6 demonstrates that variations in structural parameter exert a greater effect on tip amplitude response than on stirring force response. Among the parameters, the slit beam thickness exhibited the highest sensitivity

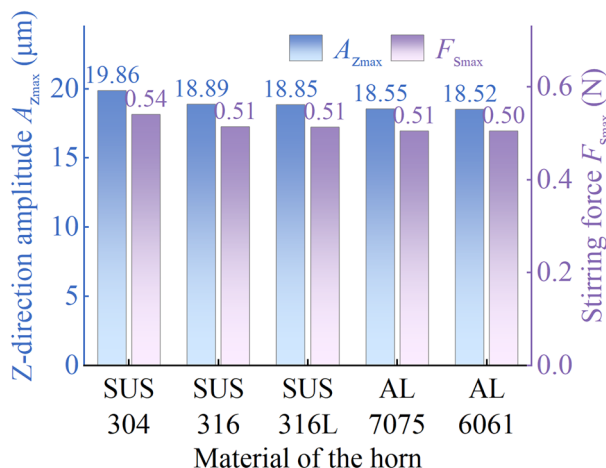


Fig. 10. Effect of horn materials on tip vibration response of the micro-actuator.

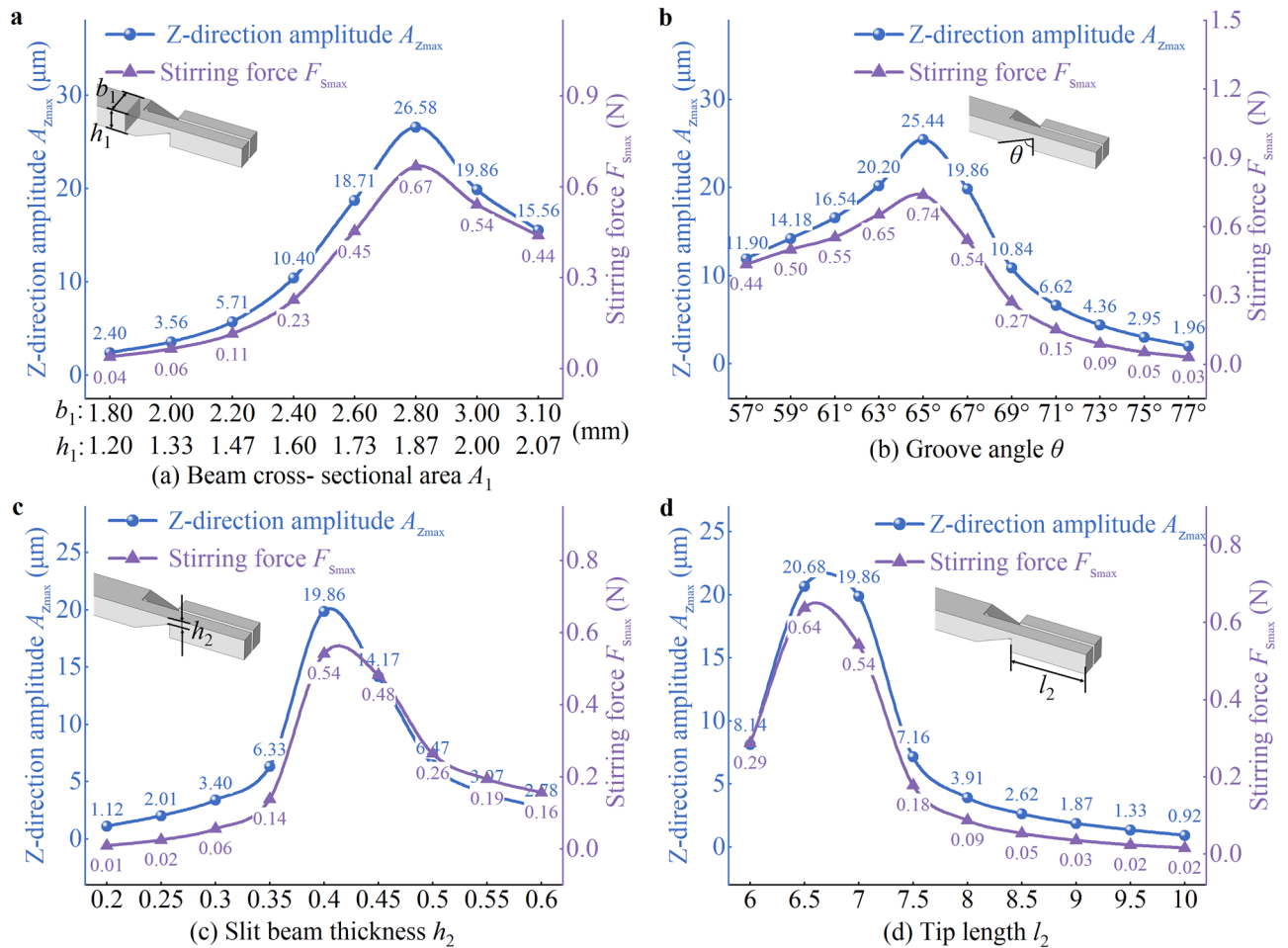


Fig. 11. Effect of different micro-actuator structural parameters on tip vibration.

Response	S_A	S_θ	S_{h_2}	S_{l_2}
Amplitude A_{zmax}	1.3789	1.2738	1.4834	1.1494
Stirring force F_{smax}	1.3681	1.2374	1.4073	1.1315

Table 6. Sensitivity analysis results.

indices (1.4834 and 1.4073), while the tip length exhibited minimal sensitivity (1.1494 and 1.1315). This indicates that the slit beam thickness dominates the tip response dynamics of the micro-actuator. Consequently, optimizing slit beam thickness should be prioritized to enhance stirring performance.

Response surface experimental design

Response surface experimental design seeks an optimal solution by fitting a multivariate quadratic regression equation which acts as a function of the influencing factors and the response values. RSMs include central composite design (CCD), Box-Behnken design (BBD), and homogeneous design. CCD is a full factorial design enhanced by the addition of a series of “star points” at the core, which help more accurately assess the quadratic effects of the system⁴³. Therefore, in this paper, CCD was chosen, and the quadratic expression is as follows:

$$y = \alpha_0 + \sum_{i=1}^k \alpha_i x_i + \sum_{i=1}^k \alpha_{ii} x_i^2 + \sum_{1 \leq i < j \leq k} \alpha_{ij} x_i x_j \quad (13)$$

where α is the coefficient to be determined; k is the number of influencing factors; x_1 is the beam cross sectional area A_1 , mm²; x_2 is the angle of the groove θ , °; x_3 is the thickness of the slit beam h_2 , mm; x_4 is the length of the tip l_2 , mm; y_1 is the Z-direction tip amplitude A_{zmax} , μm; and y_2 is the stirring force F_{smax} , N.

The test levels were set as -2, -1, 0, 1, and 2. The ranges of the influencing factors levels were selected based on the single-factor results test presented in Fig. 11 and are given in Table 7.

Level	x_1 (mm ²)	x_2 (°)	x_3 (mm)	x_4 (mm)
-2	4.056	61	0.30	5.25
-1	4.646	63	0.35	6.00
0	5.236	65	0.40	6.75
1	5.826	67	0.45	7.50
2	6.417	69	0.50	8.25

Table 7. RSM factor levels.

Test number	Impact factor				Response value	
	x_1 (mm ²)	x_2 (°)	x_3 (mm)	x_4 (mm)	y_1 (μm)	y_2 (N)
1	5.236	65	0.30	6.75	6.03	0.106
2	4.646	67	0.35	7.50	4.48	0.084
3	5.826	63	0.35	7.50	5.41	0.117
4	5.236	65	0.40	8.25	4.43	0.093
5	5.826	63	0.45	6.00	3.88	0.157
6	4.646	63	0.45	7.50	8.04	0.243
7	5.236	69	0.40	6.75	26.52	0.757
8	4.646	63	0.35	6.00	6.99	0.196
9	4.646	67	0.45	7.50	14.25	0.458
10	5.826	67	0.35	6.00	22.73	0.629
11	5.236	65	0.50	6.75	4.13	0.155
12	4.056	65	0.40	6.75	6.53	0.165
13	5.236	65	0.40	5.25	3.23	0.135
14	5.236	65	0.40	6.75	12.18	0.300
15	5.826	63	0.45	7.50	16.58	0.575
16	5.236	65	0.40	6.75	12.98	0.382
17	5.826	67	0.45	7.50	29.85	0.886
18	4.646	63	0.35	7.50	7.01	0.109
19	5.236	61	0.40	6.75	8.59	0.305
20	6.416	65	0.40	6.75	29.05	1.022
21	5.826	67	0.35	7.50	3.80	0.084
22	5.826	63	0.35	6.00	12.95	0.515
23	4.646	63	0.45	6.00	2.42	0.095
24	5.826	67	0.45	6.00	6.30	0.245
25	4.646	67	0.45	6.00	3.51	0.126
26	4.646	67	0.35	6.00	10.62	0.258

Table 8. FE simulation results.

In this paper, the Z-direction amplitude $A_{z_{\max}}$ and the stirring force $F_{s_{\max}}$ at the tip of the micro-actuator were used to assess the stirring performance of the micro-actuator; the larger their values, the higher the stirring efficiency. Based on the parameter settings of the test factor levels in Table 7, 26 groups with different factor combinations were used to perform the response surface test design. The FE simulation results for each group are shown in Table 8.

Since $y_{1_{\max}}/y_{1_{\min}}=12.31>10$ and $y_{2_{\max}}/y_{2_{\min}}=12.23>14$, a reasonable conversion of the response values is required when the extreme ratio exceeds 10^{44} . In this paper, the response values y_1 and y_2 were converted into $1/y_1$ and $1/y_2$, respectively. The simulation data in Table 8 were analyzed by analysis of variance (ANOVA) and tested for significance; the results are presented in Table 9. Note: ** denotes highly significant (p-value < 0.0001); * denotes significant (0.0001 < p-value < 0.05); - denotes no significance (p-value > 0.05).

The significance test results for the model based on $1/y_1$ yielded an F-value of 166.02, while for $1/y_2$, the F-value was 68.93, both with p-values < 0.0001, indicating the high significance of the model for analysis. The impact sequence of factors on $1/y_1$ was $x_1 > x_4 > x_2 > x_3$ (beam cross-sectional area A_1 > tip length l_2 > groove angle θ > slit beam thickness h_2), while for $1/y_2$, it was $x_1 > x_3 > x_4 > x_2$ (beam cross-sectional area A_1 > slit beam thickness h_2 > tip length l_2 > groove angle θ). The lack-of-fit term values for the $1/y_1$ and $1/y_2$ models were 0.2560 (>0.05) and 0.6058 (>0.05), respectively, indicating minimal differences between the models and the simulation data, thereby enabling regression equation analysis. The variation coefficient reflects the dispersion level of the model, with values above 15% indicating a high degree of dispersion and the need for retesting⁴⁵. The variation coefficient for the $1/y_1$ and $1/y_2$ models were 6.60% (<15%) and 10.37% (<15%), respectively,

	1/y ₁ mode			1/y ₂ mode		
Source	F-value	P-value	Significance	F-value	P-value	Significance
Mode	166.02	<0.0001	**	68.93	<0.0001	**
x ₁	170.42	<0.0001	**	96.55	<0.0001	**
x ₂	59.95	<0.0001	**	5.89	0.0336	-
x ₃	58.70	<0.0001	**	62.08	<0.0001	*
x ₄	111.55	<0.0001	**	33.44	0.0001	*
x ₁ × x ₂	2.86	0.1186	-	1.94	0.1910	-
x ₁ × x ₃	72.65	<0.0001	**	5.32	0.0416	*
x ₁ × x ₄	85.89	<0.0001	**	16.66	0.0018	*
x ₂ × x ₃	88.26	<0.0001	**	27.51	0.0003	*
x ₂ × x ₄	89.11	<0.0001	**	19.50	0.0010	*
x ₃ × x ₄	983.73	<0.0001	**	453.09	<0.0001	**
x ₁₂	2.08	0.1770	-	1.08	0.3217	-
x ₂₂	0.0765	0.7872	-	1.40	0.2624	-
x ₃₂	161.53	<0.0001	**	83.16	<0.0001	**
x ₄₂	377.56	<0.0001	**	125.11	<0.0001	**
Lost proposal	8.87	0.2560	-	1.26	0.6058	-
	R ² =0.9953			R ² =0.9887		
	R ² _{Adj} =0.9893			R ² _{Adj} =0.9744		
	R ² _{Pred} =0.9730			R ² _{Pred} =0.9365		
	Signal-to-noise ratio =49.2969			Signal-to-noise ratio =23.6119		
	Variation coefficient =6.60%			Variation coefficient =10.37%		

Table 9. ANOVA results.

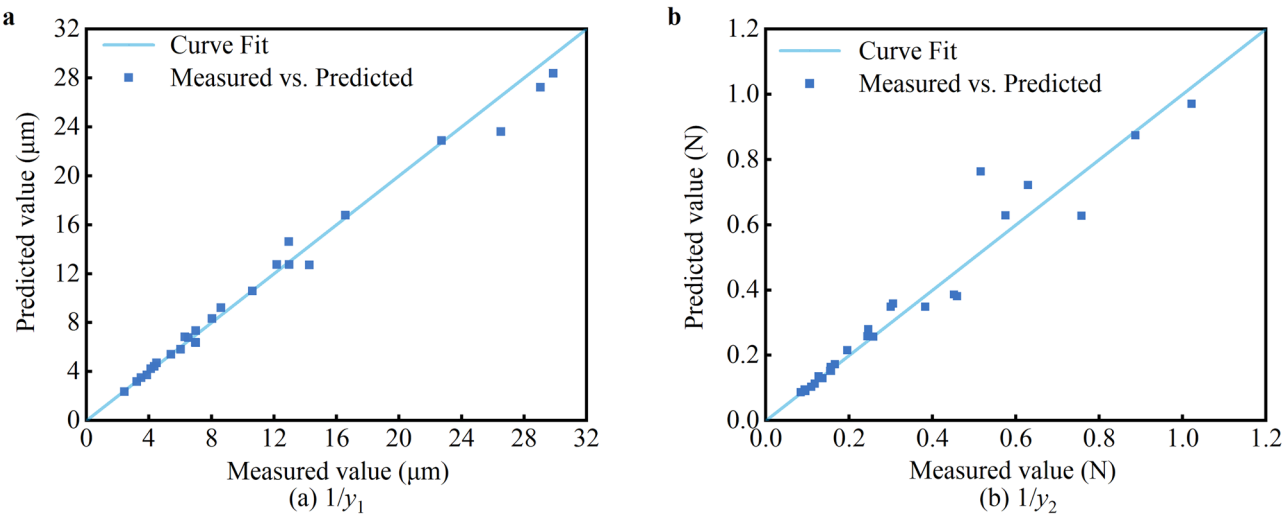


Fig. 12. Comparison between measured and predicted values of the RSM.

demonstrating high reliability. The signal-to-noise ratio (SNR) reflects the precision of a model. The SNR values for the 1/y₁ and 1/y₂ models were 49.2969 (>4) and 23.6119 (>4), respectively, indicating accurate experimental value predictions.

Figure 12 illustrates the distribution patterns between measured and predicted values in the model, with 1/y₁ and 1/y₂ used as the response values. The linear fit correlation coefficients between predicted and actual values for 1/y₁ and 1/y₂ were 0.9730 and 0.9365, respectively, indicating a strong linear correlation and close agreement between the two. Furthermore, the residuals of the regression model were distributed near the straight line of normal probability, indicating minimal differences between measured and predicted values. The following quadratic regression equations for 1/y₁ (Eq. 14) and 1/y₂ (Eq. 15) were obtained through response surface model analysis.

$$1/y_1 = 2.955 - 0.4563x_1 - 0.0178x_2 + 24.255x_3 - 1.64x_4 + 0.0036x_1x_2 - 0.738x_1x_3 + 0.054x_1x_4 - 0.24x_2x_3 + 0.016x_2x_4 - 2.136x_3x_4 + 0.01x_1^2 - 0.0002x_2^2 + 12.432x_3^2 + 0.084x_4^2 \quad (14)$$

$$1/y_2 = -81.04 - 21.68x_1 + 4.4x_2 + 677.77x_3 - 37.754x_4 + 0.169x_1x_2 - 11.205x_1x_3 + 1.322x_1x_4 - 7.52x_2x_3 + 0.422x_2x_4 - 81.378x_3x_4 + 0.409x_1^2 - 0.041x_2^2 + 500.697x_3^2 + 2.729x_4^2 \quad (15)$$

The interaction effects of the beam cross-sectional area A_1 , groove angle θ , slit beam thickness h_2 , and tip length l_2 on the Z-direction tip amplitude $A_{z_{\max}}$ were analyzed and the results are presented in Fig. 13. In Fig. 13a, the interaction between the beam cross-sectional area A_1 and the groove angle θ was not significant. All interaction response surfaces in Fig. 13b–e exhibited convex shapes. More specifically, in Fig. 13b, when the groove angle is 66° and the tip length is 6.75 mm with a fixed cross-sectional area A_1 , the Z-direction tip amplitude $A_{z_{\max}}$ increases first with increasing slit beam thickness h_2 , peaks around $h_2 = 0.40$ mm, and then decreases. The slit beam thickness affects the longitudinal wave attenuation and the tip structural stiffness; thin slit beams may hinder wave propagation to the tip, while thick beams increase tip stiffness, dampening beam vibration. In Fig. 13f, with $h_2 = 0.35$ mm and all other parameters fixed, the tip length l_2 exhibits a negative correlation with the Z-direction tip amplitude. This is due to that increasing l_2 adds mass to the slit beam, which may impede the tip vibration in the micro-actuator.

The interaction effects on the stirring force $F_{s_{\max}}$ are illustrated in Fig. 14. The patterns in Fig. 14 correspond to those in Fig. 13, exhibiting similar trends where the scissor-like mode vibration frequency of the micro-actuator slightly varies with changes in structural parameters. Consequently, the peak values of the interactions in Fig. 14 are somewhat shifted relative to those in Fig. 13.

Multi-objective optimization

Through RSM, it was observed that the tip amplitude of the micro-actuator was at the micron level. Such small high-frequency vibrations at the tip do not cause damage to the vessel wall during thrombolysis. Nevertheless, the tip amplitude y_1 and stirring force y_2 of the micro-actuator cannot reach their optimal values simultaneously. Therefore, a MOO design approach should be utilized to coordinate them closely towards optimality, aiming to develop a micro-actuator able to achieve large tip amplitudes and strong stirring forces in the scissor-like mode.

The MOO problem addressed in this paper can be formulated as follows. The tip amplitude and stirring force of the micro-actuator must be maximized under the constraints of the beam cross-sectional area x_1 , groove angle x_2 , slit beam x_3 , and tip length x_4 . The mathematical model is as follows:

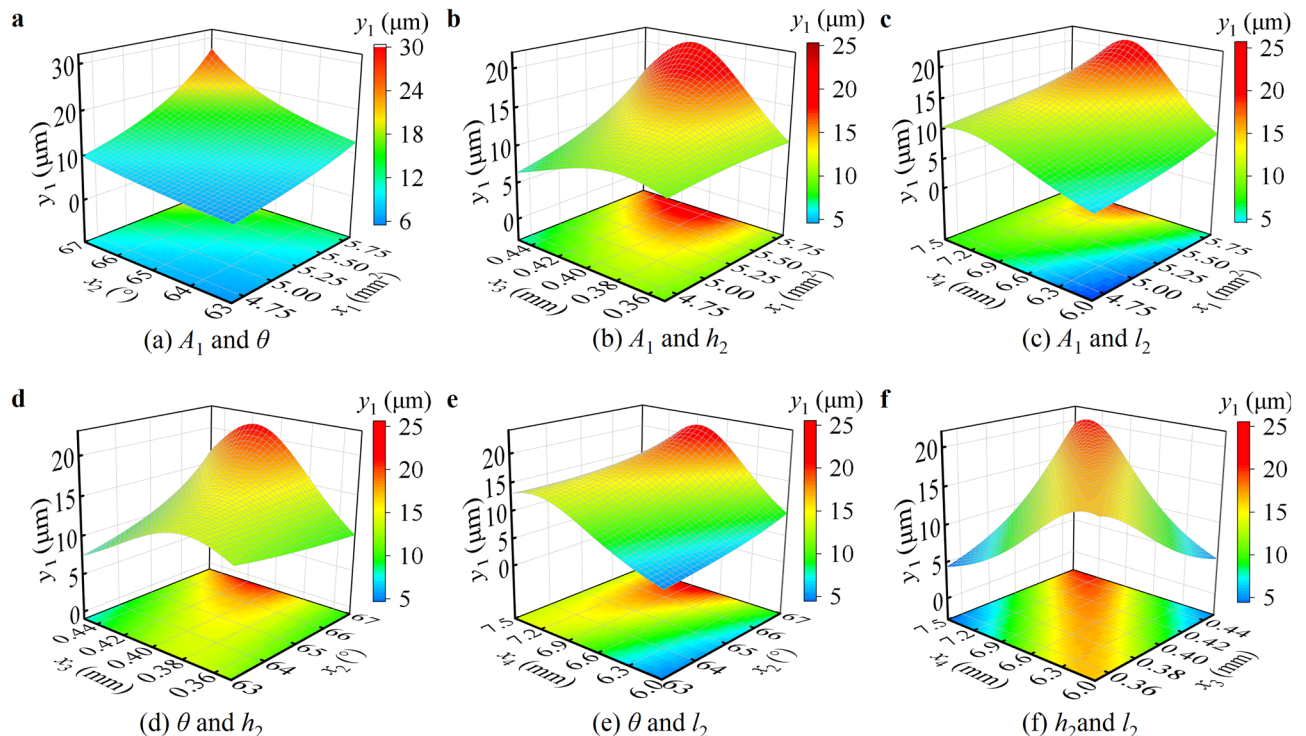


Fig. 13. Response surfaces of the interaction effects of different parameters on the y_1 model.

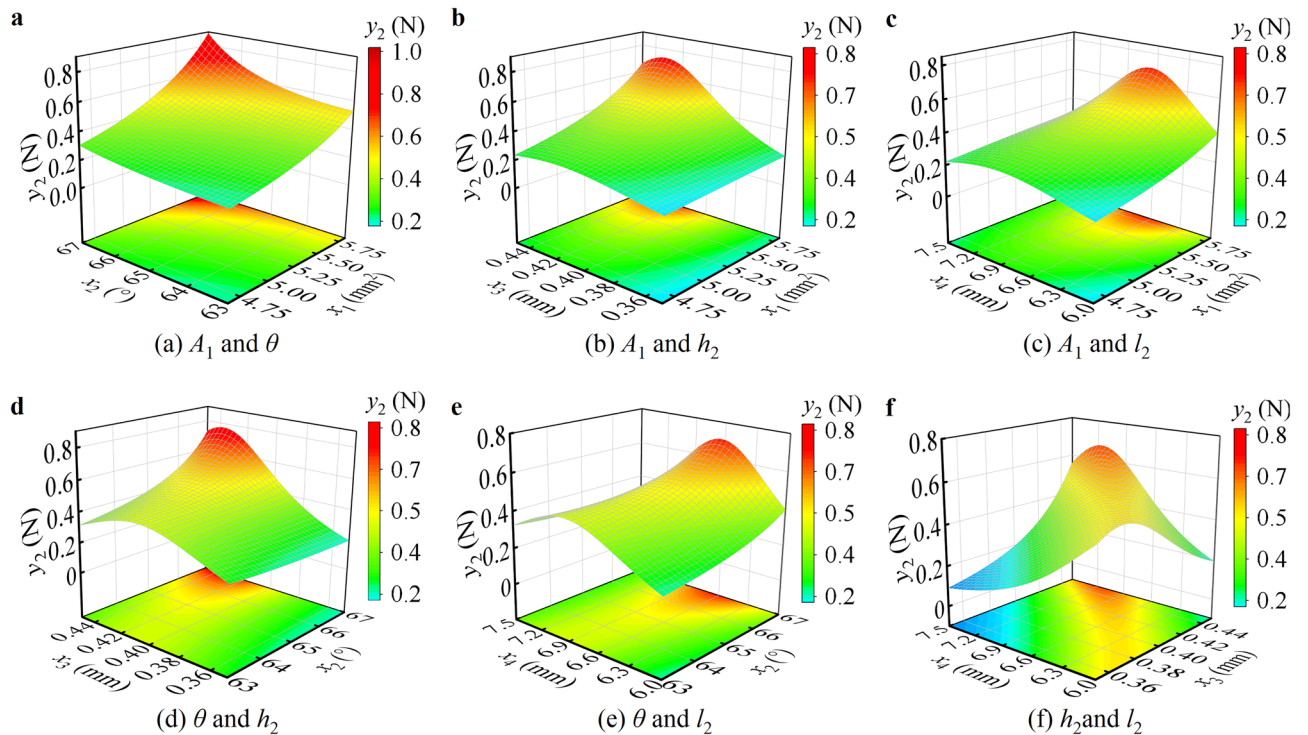


Fig. 14. Response surfaces of the interaction effects of different parameters on the y_2 model.

$$\begin{aligned}
 &\text{Maximum: } F(X) = [y_1(X), y_2(X)]^T \\
 &X = [x_1, x_2, x_3, x_4]^T \\
 &\text{Subject to :} \\
 &4.056 \text{ mm}^2 \leq x_1 \leq 6.417 \text{ mm}^2 \\
 &61^\circ \leq x_2 \leq 69^\circ \\
 &0.30 \text{ mm} \leq x_3 \leq 0.50 \text{ mm} \\
 &5.25 \text{ mm} \leq x_4 \leq 8.25 \text{ mm}
 \end{aligned} \tag{16}$$

where $y_1(X)$ is the amplitude function at the tip of the micro-actuator (Eq. 13); $y_2(X)$ is the stirring force amplitude function at the tip of the micro-actuator (Eq. 14); x_1 is the beam cross-sectional area, A_1 , mm^2 , x_2 is the groove angle, θ , $^\circ$; x_3 is the slit beam thickness, h_2 , mm; and x_4 is the tip length, l_2 , mm.

Currently, commonly used MOO algorithms include MOAHA, MOPSO, NSGA, the improved NSGA-II, and the enhanced NSGA-III⁴⁶. MOAHA balances multiple objective functions by simulating the efficient foraging strategies of hummingbirds, generating a set of well-distributed Pareto-optimal solutions. However, this behavioral simulation requires frequent objective function evaluations, resulting in computationally intensive processes⁴⁷. MOPSO introduces a disturbance factor to enhance algorithm convergence and diversity; however, it suffers from a poor local search capability, leading to potential local optima and low search accuracy⁴⁸. NSGA is based on the initial population and performs non-dominated sorting and crowding degree calculation. It uses genetic operations to generate offspring, merges and updates the population, and iteratively approaches the Pareto front of multi-objective optimization to obtain non-dominated solutions⁴⁹. In contrast, NSGA-II incorporates an elite strategy and employs crowding distance instead of a predefined shared radius fitness sharing strategy to improve population diversity. NSGA-III (Fig. 15) enhances convergence and diversity in solving super MOO problems by incorporating a reference point mechanism⁵⁰.

For MOO problems, the task is to find the best compromise solutions in the design space, namely the Pareto-optimal solution set. This study compared MOO using the NSGA-II and NSGA-III algorithms. The parameter settings for the two algorithms are listed in Table 10; all other parameters were set to default values. Each algorithm was run three times, and the average Pareto-optimal solution set was taken to compare the MOO results, as shown in Fig. 16. The convergence process of the two algorithms is presented in Fig. 17.

As depicted in Fig. 17, NSGA-III demonstrates smoother convergence curves with smaller fluctuations for objectives y_1 and y_2 compared to NSGA-II. For y_1 convergence (Fig. 17a), NSGA-III achieves convergence after approximately 60 generations whereas NSGA-II requires about 90 generations. Similarly, y_2 convergence (Fig. 17b) occurs at 70 generations for NSGA-III versus 100 generations for NSGA-II, confirming the superior convergence speed of NSGA-III. Notably, both algorithms stabilize along a linear trajectory after convergence, indicating equivalent optimization accuracy.

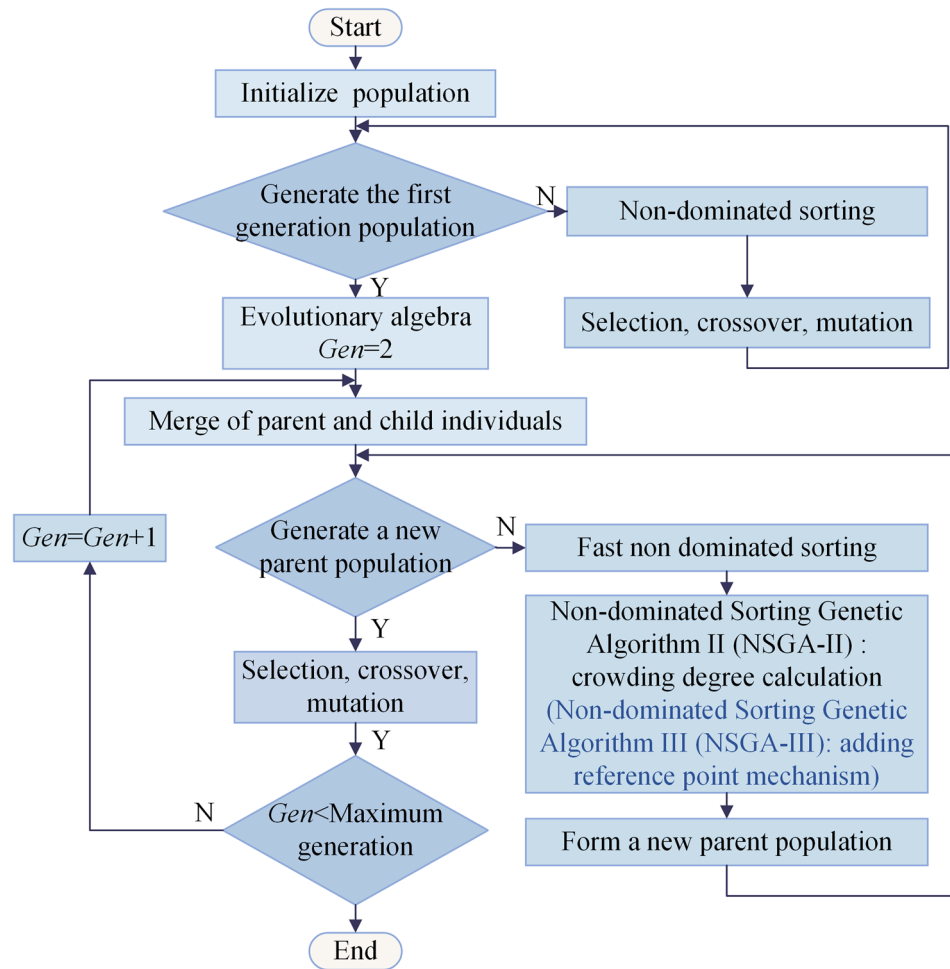


Fig. 15. NSGA-III algorithm flowchart.

Parameters	NSGA-II	NSGA-III
Population	150	150
Number	500	500
Crossover rate	90%	90%
Mutation rate	10%	10%
Reference points	–	2

Table 10. Algorithm parameters.

The Pareto fronts obtained from MOO using the two algorithms generally lied along a single curve. The optimal solution set of NSGA-III exhibited greater diversity and a more evenly distributed range than NSGA-II, making it better suited for various weighted decision scenarios. As regards NSGA-II, the Pareto-optimal solution set yielded a range of [32.34 μm , 34.24 μm] for the Z-direction tip amplitude and [1.267 N, 1.328 N] for the stirring force. On the contrary, the Pareto-optimal solution set from NSGA-III yielded a range of [32.35 μm , 34.35 μm] for the Z-direction tip amplitude and [1.233 N, 1.328 N] for the stirring force. The stirring force amplitude ranges obtained by both algorithms met the force requirements for thrombus fragmentation. Hence, selecting the maximum y_1 value as the Pareto-optimal solution for both algorithms yielded similar optimal structural parameter values: $x_1 = 5.826 \text{ mm}^2$, $x_2 = 67^\circ$, $x_3 = 0.45 \text{ mm}$, and $x_4 = 7.17 \text{ mm}$. FE simulations using these optimal structural parameters were conducted to validate the results against the optimal solutions from both algorithms, as shown in Table 11. The relative error equation is given as follows:

$$\delta = \frac{|A_1 - A_2|}{A_1} \times 100\% \quad (17)$$

where δ is the error value; A_1 is the test value; A_2 is the predicted value.

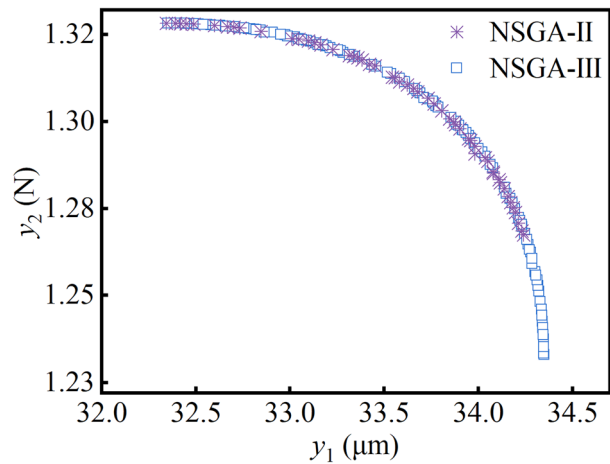


Fig. 16. Comparison of Pareto Front of the two algorithms.

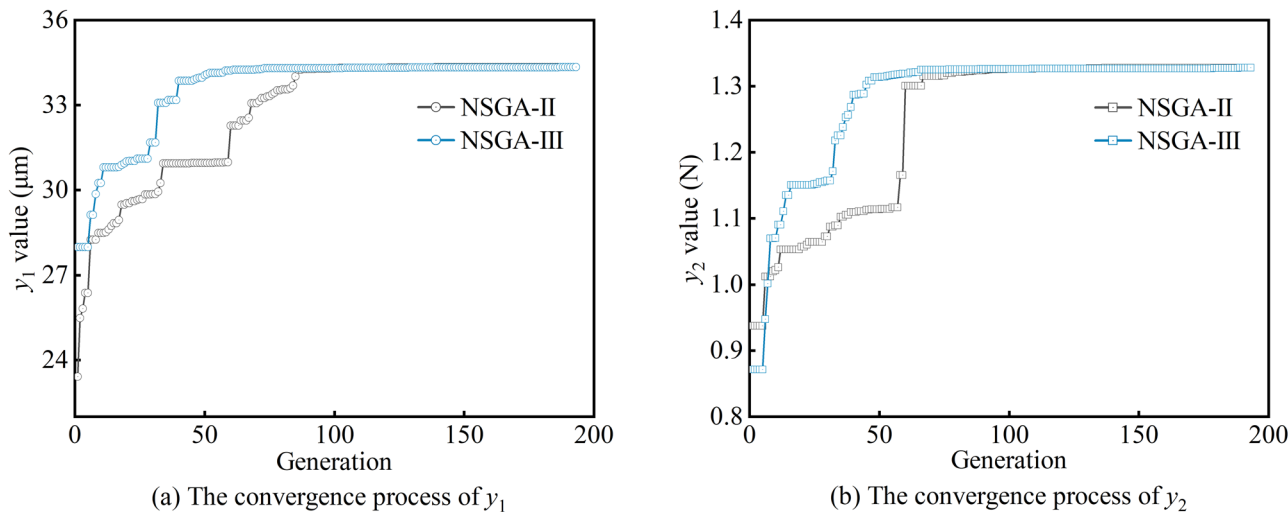


Fig. 17. Comparison of the convergence processes of the two algorithms.

	Z-direction amplitude y_1 (μm)			Amplitude of stirring force y_2 (N)		
	Experimental value	Projected value	Errors (%)	Experimental value	Projected value	Errors (%)
NSGA-II	35.62	34.24	3.88	1.251	1.167	7.19
NSGA-III	35.62	34.35	3.56	1.251	1.189	5.21

Table 11. Comparison of validation results.

The prediction errors of both algorithms for the y_1 and y_2 models were less than 10%, indicating that the optimization model has high prediction accuracy and stability. Moreover, the NSGA-III algorithm is more suitable for identifying the optimal solution for this optimization model. Compared to the initial model ($x_1=6.0\text{ mm}^2$, $x_2=67^\circ$; $x_3=0.4\text{ mm}$; $x_4=7.0\text{ mm}$) with a maximum amplitude of $19.86\text{ }\mu\text{m}$ and maximum stirring force of 0.54 N , the optimized micro-actuator tip exhibited a 79.35% increase in maximum amplitude and a 131.66% increase in maximum stirring force.

Prototype performance verification

A prototype model was manufactured based on the optimal structural parameter combination, as shown in Fig. 18a. The transducer and micro-actuator were bonded using a metal adhesive, with a four-layer piezoelectric stack with dimensions of $\phi 38\text{ mm}\times\phi 13\text{ mm}\times 6.35\text{ mm}$ embedded in a pre-tensioned structure to apply the driving voltage. The polarization direction of the piezoelectric stack aligned with the length direction of the actuator. The experimental platform principle is illustrated in Fig. 18b. The experimental procedure begins by

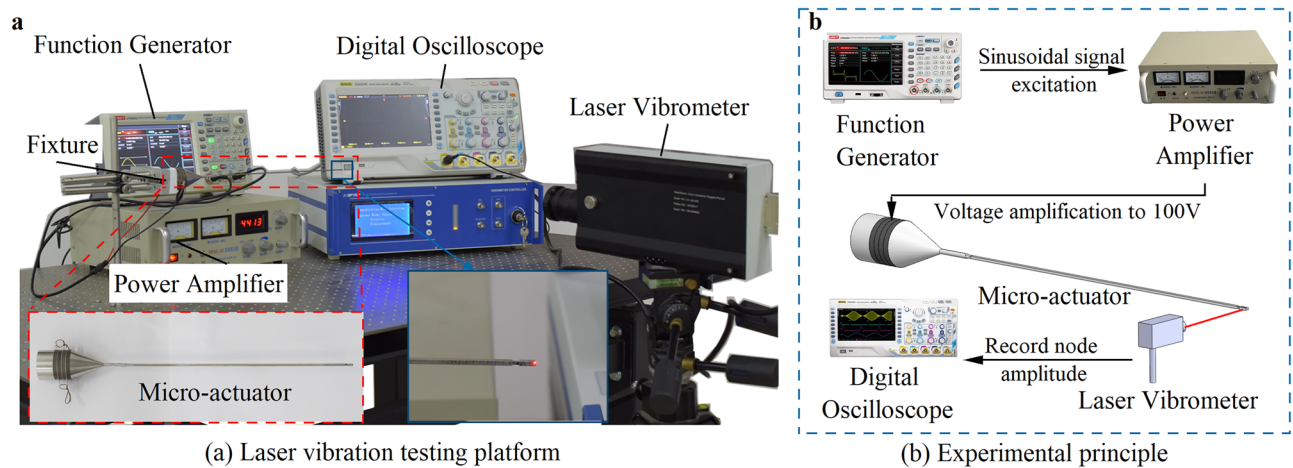


Fig. 18. Test platform and schematic diagram of the experimental principle.

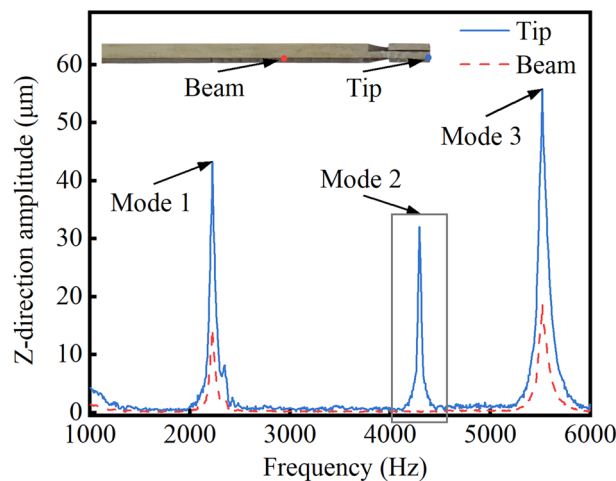


Fig. 19. Transverse amplitudes of the micro-actuator tip and beam.

first measuring the resonance frequency of the device and then inputting the resonance frequencies within the scanning range into function generators to measure the device amplitudes under different modes.

The input signal of the micro-actuator was generated by a function generator (UTG4082A) and amplified to 100 V by a power amplifier (HEAS-100). A laser vibrometer (LV-S01-KH) was placed on one side of the micro-actuator tip to measure the amplitudes at different locations. The transducer horn was horizontally fixed at the left end using a fixture. The positive and negative poles of the transducer were connected to the power amplifier. The scanning frequency ranged was set from 1000 to 6500 Hz. When the amplitude reached its peak, the entire device was in a state of harmonic vibration. The measurement results are depicted in Fig. 19.

The resonance frequencies of the micro-actuator prototype were found to be 2224.7 Hz, 4290.2 Hz, and 5517.5 Hz. Additional measurements of the actual modes of the prototype were performed by sequentially setting the function generator frequencies to the resonance frequencies of the device. The amplitudes at the nodes on both sides of the micro-actuator were measured by horizontally moving the laser vibrometer at equidistant intervals. The distance between adjacent measurement points at the actuator tip was 1 mm, while that between adjacent measurement points on the beam was 4 mm. The amplitudes of all nodes were recorded using a digital oscilloscope (DS4024E), the peak amplitudes at each node were noted, and the true mode shapes of the prototype were visualized by connecting the points. The measurement results are illustrated in Fig. 20.

The experimental results demonstrated the successful excitation of the scissor-like mode of the micro-actuator at 4290.2 Hz, closely matching the FE-predicted value (4254.8 Hz). In the scissor-like mode, minimal vibration occurred at the nodes along the micro-actuator beam, with amplitude predominantly occurring at the tip. The Z-direction amplitude at the tip was 32.04 μm . Compared to the previously designed scaled micro-actuator prototype¹², the tip amplitude under an excitation of 5 V increased by 119 times (0.267 μm). This improvement can be attributed to the following reasons. First, the conical transducer effectively amplifies the longitudinal vibrational energy generated by the transducer, thereby increasing the response at the micro-actuator tip. Subsequently, the application of MOO to optimize the structural parameters of the micro-actuator

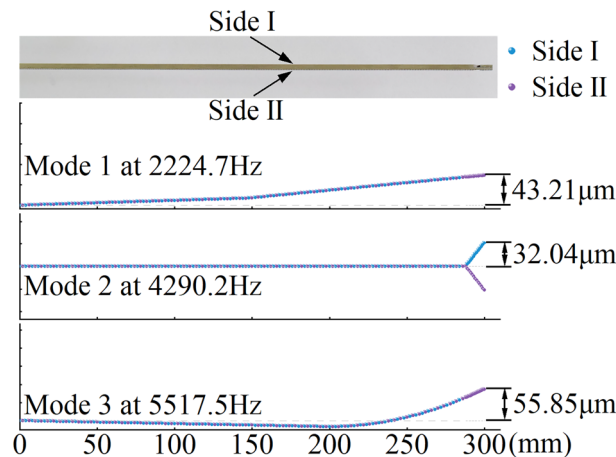


Fig. 20. Mode shape of the micro-actuator.

significantly enhances its stirring performance. It is worth noting that due to the stringent size constraints of the micro-actuator in the vascular environment, the structural optimization investigated in this study lays the foundation for future micro-actuators to generate optimal amplitude and stirring force in smaller blood vessels.

The Z-direction amplitude at the tip of the micro-actuator prototype differs from the FE result of the optimal structure (35.62 μm) by 10.05%. The analysis results suggest that the required vibration modes for the micro-actuator prototype may be affected by the complex boundary conditions, as well as manufacturing and assembly errors. Using Eq. (10), the maximum stirring force at the tip of the micro-actuator prototype was calculated as 0.973 N. The maximum amplitude and maximum stirring force of the initial model ($x_1 = 6.0 \text{ mm}^2$, $x_2 = 67^\circ$; $x_3 = 0.4 \text{ mm}$; $x_4 = 7.0 \text{ mm}$) were 19.86 μm and 0.54 N, respectively. After optimization, these values were successfully improved by 61.33% and 80.19%, respectively, suggesting that the micro-actuator can be designed with a smaller size and operated at lower safety driving voltage for small vessels.

Discussion

In this paper, a Response Surface Methodology Non-dominated Sorting Genetic Algorithm III (RSM-NAGA-III) optimization model for Multi-Objective Optimization (MOO) of a fragmented thrombolytic micro-actuator has been developed. The decisive variables included the groove angle θ , beam cross-sectional area A_1 , slit beam thickness h_1 , and tip length l_2 . The optimization objectives included the maximum tip amplitude and the maximum stirring force. Central composite design (CCD) was used to design experiments for the variables, a quadratic regression model was constructed based on the Response Surface Methodology (RSM), MOO was performed using the Non-dominated Sorting Genetic Algorithm II (NAGA-II) and Non-dominated Sorting Genetic Algorithm III (NAGA-III), and the corresponding optimal structural parameters were determined by analyzing the Pareto front based on the preferred amplitude principle. The main conclusions are as follows:

- (1) The dimensions of the horn for different materials were determined using the equation for horn frequency, combined with the dynamics model of the fragmented thrombolytic micro-actuator. The influencing factors included the groove angle θ , beam cross sectional area A_1 , slit beam thickness h_2 , and tip length l_2 . Single-factor analyses were conducted for each influencing factor. Through Sobol sensitivity analysis, it was revealed that the slit beam thickness h_2 has the strongest effect on the response at the micro-actuator tip, while the tip length l_2 has the weakest effect.
- (2) The experimental design was conducted using CCD to establish the RSM quadratic regression model. R^2 test was performed on the test results. The $1/y_1$ model results were: $R^2 = 0.9953$, $R_{Adj}^2 = 0.9893$, $R_{Pred}^2 = 0.9730$; the $1/y_2$ model results were: $R^2 = 0.9887$, $R_{Adj}^2 = 0.9744$, $R_{Pred}^2 = 0.9365$. The results indicated that the regression model has high accuracy and adaptability in predicting the tip amplitude and stirring force of the micro-actuator.
- (3) The relative error of NSGA-II was 3.88% for the y_1 model and 7.19% for the y_2 model; the relative error of NSGA-III was 3.56% for the y_1 model and 5.21% for the y_2 model. The NSGA-III algorithm was found to be more suitable for identifying the optimal solution of the optimization model for the fragmented thrombolytic micro-actuator structural parameters.
- (4) In the optimal solution of the Pareto Front obtained by NSGA-III, the maximum amplitude and maximum stirring force at the tip of the optimized micro-actuator increased by 79.35% and 131.66%, respectively. The maximum amplitude of the tip of the micro-actuator prototype fabricated based on the optimal structural parameters was 32.04 μm , and the actual amplitude is improved by 61.33%. The error between the actual and finite element (FE)-predicted amplitude values was 10.05%. The maximum stirring force at the tip of the micro-actuator prototype was 0.973 N, and the actual amplitude increased by 80.19%. The error between the actual and FE-predicted stirring force values was 22.22%.

- (5) The proposed RSM-NAGA-III-based structural parameter optimization model can improve the stirring performance of fragmented thrombolytic micro-actuators. This study primarily focused on the structural parameter optimization of fragmented thrombolytic micro-actuators. Future research will explore the following areas for refinement and standardization: (a) Additional structural parameters of the micro-actuator and their interactions will be considered; (b) An adaptive control system based on real-time feedback, e.g., pressure sensors, should be designed to enable dynamic adjustment of the working frequency, ensuring the stability of scissor-like mode of the micro-actuator. (c) A comprehensive evaluation standard including the vibration frequency, amplitude threshold, and energy efficiency should be developed to assist medical staff in decision-making.
- (6) It is noteworthy that the hysteresis effect of piezoelectric materials may affect the dynamic response performance of the micro-actuator. Future work will integrate sliding mode control with disturbance observers⁵¹ to develop a closed-loop compensation algorithm, aiming to optimize the vibration energy transfer efficiency of fragmented thrombolytic micro-actuators.

Data availability

Data is included in the article: For further questions, please contact the corresponding author.

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Zhuowei He: Writing - initial draft, finite element simulation, data organization. Junjie Lei: Writing - Review and Editing. Jingjing Yang: Writing - review and editing, supervision, funding acquisition, resources. Huba Zhu: Data organization and result analysis. All authors reviewed the manuscript.

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Declarations

Competing interests

The authors declare no competing interests.

Additional information

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