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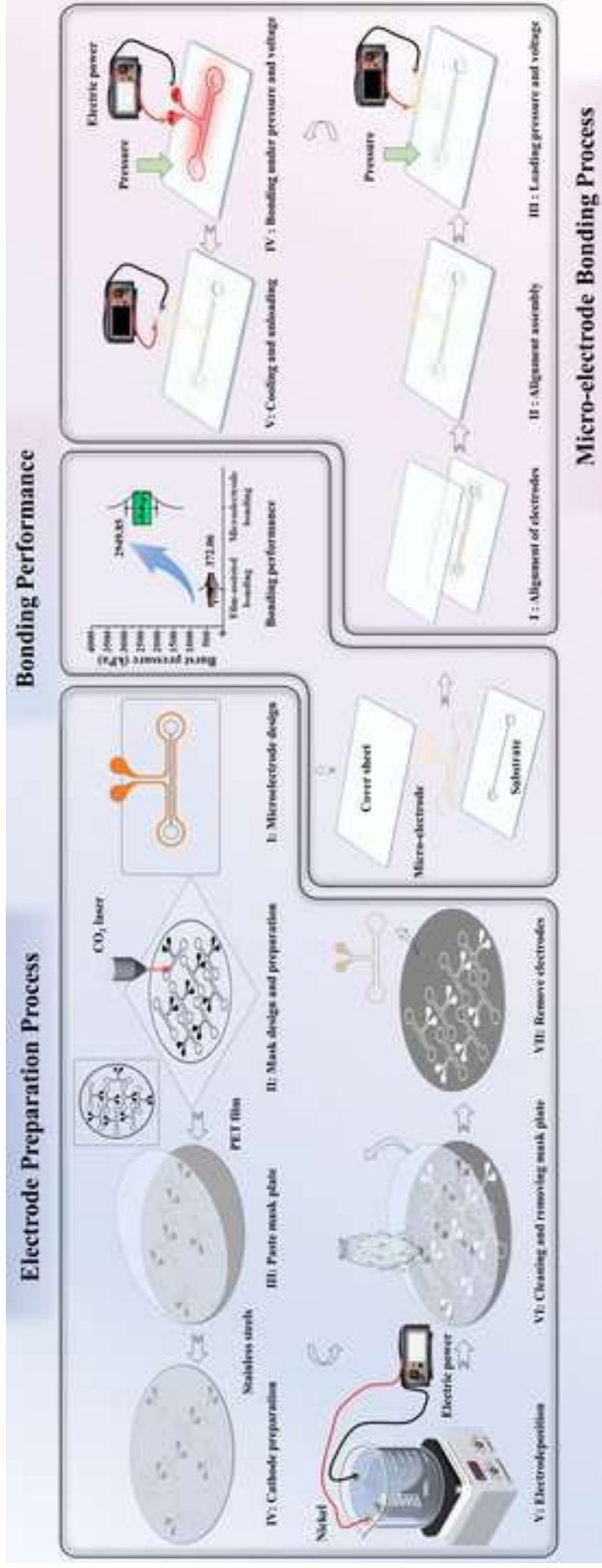
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Highlights

1. A microelectrode bonding technology for microfluidic chips is engineered.
2. Microelectrode bonding achieves sub-3V rapid sealing in 15 seconds.
3. Burst pressures exceed 2.9 MPa with minimal microchannel deformation.
4. Technology is green and uses no hazardous chemicals or produces pollutants.
5. Adaptability to various materials broadens application scope.

1 **An innovative patternable microelectrode bonding technology for**
2 **high-performance and cost-effective sealing in microfluidic chips**

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16

17 **Abstract**

18 Microfluidic chips pose as an interdisciplinary frontier as they integrate various fields, while
19 typically serving as a novel technological platform for precise manipulation of minute liquid
20 volumes and biological analysis. However, the chase for enhanced bonding quality in order to
21 fabricate these chips correctly, has led to the use of increasingly complex technology, limiting the
22 marketability of microfluidic products. In this work, a novel microelectrode bonding technology
23 is proposed, which addresses the demands for reliable, low-cost, and high-throughput bonding.
24 The proposed process utilizes the Joule heating effect of microelectrodes at low voltages, in order
25 to rapidly generate sufficient heat and allow for the successful bonding of the chip. The material
26 used for the microelectrodes is nickel, and the method chosen for their fabrication is small-batch
27 electrodeposition. The microelectrodes and microchannels morphology are characterized by
28 Extended Depth of Field Microscopy, while the quality of heating produced is assessed by a high-
29 speed infrared camera. The finalized bonding strength is characterized by measuring the
30 microchannel burst pressure, using an apparatus comprising of a syringe pump, a precision
31 pressure gauge, and a connecting tubing. The results prove that this is a rapid polymer bonding
32 method, which uses less than 3 Volts. Additionally, the results underscore the process's
33 effectiveness, yielding chips with burst strengths over 2.9 MPa, while microchannel deformations
34 are kept under 10%. Finally, the advantages of the technology are discussed and its limitations are
35 eliminated by further conceptualization. The proposed method uses no chemicals or contaminants,

36 nor complex equipment, rendering it simple, green, and sustainable. This paves the way for the
37 development of new efficient and greener paradigms, aiming towards leading engineering and
38 manufacturing to a sustainable future.

39

40 **Keywords:** Microfluidics; Microfabrication; Bonding technology; Polymers; Sealing;

41 Microelectrode bonding

42 **1 Introduction**

43 Microfluidic technology has emerged as a pivotal advancement in the biomedical and
44 chemical analysis sectors, and is epitomized by microfluidic chips [1–3]. A microfluidic chip is a
45 miniature device that integrates microchannel networks and micro-mechanical structures, designed
46 for precise control of the movement and reactions of minute amounts of fluids and particles at the
47 micrometer scale [4,5]. These devices integrate micro-nano technology with biomedical sciences,
48 and offer numerous advantages, i.e. high efficiency [6–8], precision and control [9,10],
49 miniaturization [11], and the capacity for complex analyses and syntheses [12,13] on a single
50 platform [14,15]. Applications span from drug delivery systems and diagnostic assays, to
51 environmental monitoring and lab-on-chip devices, demonstrating their versatility and
52 significance in advancing biomedical, and analytical research [16,17].

53 Nowadays, microfluidic technology has reached its maturity stage, with a substantial number
54 of devices successfully transitioning from prototypes to commercialized products [10,18].
55 Typically, the production of microfluidic chips involves intricate and critical processes regarding
56 design, verification, manufacturing, which include bonding. The marketization and widespread
57 adoption of microfluidics is however dependent on the further development and the
58 standardization of efficient and reliable bonding technologies to improve the sustainability of the
59 field [19]. At this stage, there is a pressing need for reliable, cost-effective, and high-volume
60 thermoplastic bonding methods with improved sustainability. For polymeric microfluidics,

61 polydimethylsiloxane (PDMS) and thermoplastic are the two major materials, and both materials
62 present their own unique qualities in microfluidic applications [18]. Plasma bonding is typically
63 suitable for the design and validation phases of lab-scale hybrid microfluidic devices composed of
64 PDMS and glass [20]. In hybrid PDMS/glass microfluidic devices, surface hydroxylation via
65 oxygen plasma treatment, ultraviolet-ozone (UVO) treatment, or corona discharge method is the
66 main bonding technique. However, the use of plasma systems for thermoplastic polymers usually
67 leads to very weak bonding [21]. Moreover, UV exposure, ozone or oxygen plasma for
68 thermoplastic polymers has the ability to produce cytotoxic by-products, as for example hydrogen
69 peroxide, which must be avoided in most biomedical applications and cell studies [22].

70 Traditional methods for thermoplastic, i.e. adhesive bonding [23,24], solvent bonding [25,26],
71 thermal bonding [27,28], chemical bonding [29], as well as laser [30,31], and ultrasonic welding
72 [32,33], provide solutions for numerous material and application requirements. However, all these
73 methods appear to possess respective advantages and drawbacks [21].

74 The use of adhesive layers provides a rapid technology that preserves transparency, allows
75 permeability for cell culturing applications and pre-functionalization, but typically faces
76 cytotoxicity and adsorption challenges, as well as channel thickness limitations for double-sided
77 layers [5,6]. Solvent bonding poses as a low-cost, rapid approach that allows for good optical
78 transparency and robust bonding strength, especially when integrated with thermal bonding. Its
79 challenges include the necessity of use of pre-functionalized channels, channel deformation, and
80 issues rising with solvent residues [25,26]. Thermal fusion bonding is another fast method that

81 produces strong bonding, but it is limited via potential channel deformations, as well as restrictions
82 in the minimization of channel dimensions [27,28]. Chemical bonding is a method that enables
83 strong bonds employing the use of covalent bonding, while it can provide a pathway to
84 simultaneously functionalize surfaces (as for example biomolecule immobilization, or control of
85 wettability) it is considered as a complex and time-consuming process with commercialization
86 limitations [11]. Laser welding is another rapid method that allows for pre-functionalization, and
87 offers high bonding strength. However, it necessitates strict requirements for its use, i.e.
88 simultaneously transparent and absorbent layer, high clamping pressure, and good surface finish.
89 It is known that it also induces thermal stresses throughout the polymer, which can lead to
90 deformations on the microfluidic chip [30,31]. Ultrasonic welding is ultra-fast and inexpensive as
91 a technology, and is suitable for use in mass production, has high bonding strength, and allows for
92 pre-functionalizing channels prior to bonding. Unfortunately for the field, it has been proven that
93 its use occasionally leads to channel deformation, clogging, formation of gaps between bonded
94 layers, and that it constraints channel heights due to the self-induced polymer shrinkage of the
95 method [32,33]. Lei et al. introduced a microwave-based bonding technology, in which thin-film
96 metal (gold) was pre-deposited on the microfluidic chip interface using an electron beam process
97 [34]. Although this method achieved the bonding of PMMA chips at 10 W within 120 seconds, the
98 selective nature of microwaves, which is limited to materials that are relatively transparent to
99 microwaves, as well as the necessity of depositing metal films, render this approach less suitable
100 for low-cost, rapid manufacturing. Another study, achieved efficient bonding in polymer-

101 microfluidic devices by applying a 300 W high-frequency electromagnetic field and microwave
102 energy to polyaniline (a conductive polymer) [35,36]. However, the high energy consumption and
103 specialized equipment requirements appear to limit the broader application of this technology.
104 Additionally, there are more advanced and modern methods that are introduced recently, as for
105 example gas-assisted thermal bonding, which shows potential for the creation of reliable
106 microfluidic devices with thermoplastics. The biggest hurdle for using these sophisticated and
107 advanced new bonding technology is that they necessitate and require the development of
108 specialized, complex equipment that are not currently used in industry [37].

109 Thermoplastic polymers are some of the most important materials in microfluidics, however,
110 due to the diverse methods and requirements for bonding, thermoplastic adhesion always poses as
111 a significant challenge [38–40]. Researchers have highlighted this complexity and the necessity
112 for introducing innovative solutions in numerous works [18,21,41]. Given this mixed situation
113 with advantages and challenges, there is a paramount need to invent and propose a method that
114 combines the strengths of existing ones, while simultaneously manages to mitigate their limitations.
115 In an effort to find the optimum bonding methodology, Matteucci et al. compared ultrasonic
116 welding and thermal bonding for integrating thin film metal electrodes in injection molded
117 microfluidic chips, showcasing that the former bonded chips showed significantly superior
118 performance [42]. The research employed ultrasonic welding and thermal bonding technology,
119 where the thin-film metal electrodes functioned solely as sensors for analytical purposes. These
120 electrodes served as bonded objects but did not actively participate in the bonding process, not

121 taking advantage of their presence in the chip.

122 However, despite the research community's efforts to investigate ways that can extend and
123 develop further the traditional bonding technologies, breakthroughs and novel methods that can
124 become a paradigm for bonding have been scarce in literature. Evidently, it is necessary to develop
125 novel processes that can combine the need to be straightforward in their implementation, cost-
126 effectiveness, as well as flexibility and adaptability to different materials and chip designs,
127 avoiding the use of exotic equipment that would dramatically increase their cost-effectiveness.

128 The current paper, aims to address the above-mentioned challenge of bonding methods for
129 microfluidic chips and to provide a new sustainable pathway, which can become a new paradigm
130 in the field. Herein, the researchers propose and develop a novel thermoplastic microfluidic chip
131 bonding technology that is based on microelectrode heating. This new method addresses the
132 demands for sustainability, i.e. reliability, low cost, and high throughput without the need of use
133 of exotic or dangerous materials. Aiming to achieve the rapid bonding of chosen microfluidic chips,
134 a small-batch customization and electrodeposition of nickel microelectrodes is applied on top of
135 PMMA microfluidic chips. These chips are fabricated using microinjection molding. This
136 proposed method is very simple, as it does not require expensive or complex equipment, while it
137 shows potential for eradicating numerous limitations of other methods, positively influencing the
138 final manufacturing cost. The ultimate goal is to uphold high bonding strength and minimal
139 microchannel deformation. The researchers use a series of characterization methodologies to
140 validate the proposed bonding process and explore its applications, having in mind further

141 developments that can be underpinned with this for all microfluidic technology and its applications.

142 **2 Materials and Methods**

143 **2.1 Materials**

144 Poly (methyl methacrylate) (PMMA), is a low-cost polymer material that is commonly used
145 in microfluidic chips. The main material used in this work is a commercial PMMA (CM 205, Chi
146 Mei, Taiwan) whose properties are well known in literature [43]. Nickel (Ni, VALE INCO, Canada)
147 shows excellent thermal and electrical conductivity, mechanical strength, thermal stability,
148 compatibility with electrodeposition, and biocompatibility [44]. These properties make it an ideal
149 material for achieving uniform heating, precise bonding control, and consistent bonding quality in
150 microfluidic chip fabrication. Mechanical strength allows it to maintain stable shape and
151 functionality in microstructures, while its thermal stability ensures that it does not deform or suffer
152 performance degradation during bonding. As a non-precious metal, nickel is abundant, offering
153 both economic and sustainable benefits.

154

155 **2.2 Microelectrode bonding process**

156 The bonding process based on microelectrodes for microfluidic chips and is used in this work
157 is depicted in Fig. 1 (a). This process is called microelectrode bonding technology (MB) and can
158 be described as follows. Initially, the patterned microelectrodes are placed onto the substrate in
159 designated positions. Subsequently, a cover sheet is placed over the chip and the microelectrodes,

160 followed by pressure and voltage that are applied to the assembled chip. At this juncture, the
161 microfluidic chip gradually joins together, due to the heat that is generated by the microelectrodes
162 and the pressure applied. The core working principle is that when current passes through
163 microelectrodes, the resistance generates heat according to Joule's law, subsequently causing the
164 microelectrodes to increase their temperature and generate bonding energy. This temperature
165 increase is controlled by adjusting the current's magnitude and the duration of its application. This
166 heat allows for the surface locally to exceed the glass transition temperature (T_g) even up to the
167 melting temperature (T_m) of the polymer, and in combination with pressure, it allows for the fusion
168 of the substrates. Additionally, the maximum temperature of the microelectrodes can be controlled
169 by adjusting the applied voltage or duration. When the microelectrode temperature is maintained
170 between the T_g and T_m , the microchannels are primarily sealed through molecular chain diffusion
171 or entanglement [27]. At this stage, this process can be termed microelectrode bonding. However,
172 microelectrode bonding requires prolonged bonding time. When the microelectrode temperature
173 exceeds the T_m , the chip undergoes fusion welding. In summary, the bonding mechanism and
174 strength, controlled according to the application, are also distinctive attributes of this process.
175 Finally, by unloading the bonding voltage, cooling the chip back to room temperature, and
176 removing the pressure, the microelectrode bonding process is complete. The main equipment
177 employed uses a power supply and a small bench vice. This bench vice is primarily used to apply
178 pressure, which is controlled via a torque wrench. The parameters for the bonding experiment are
179 shown in Table 1.

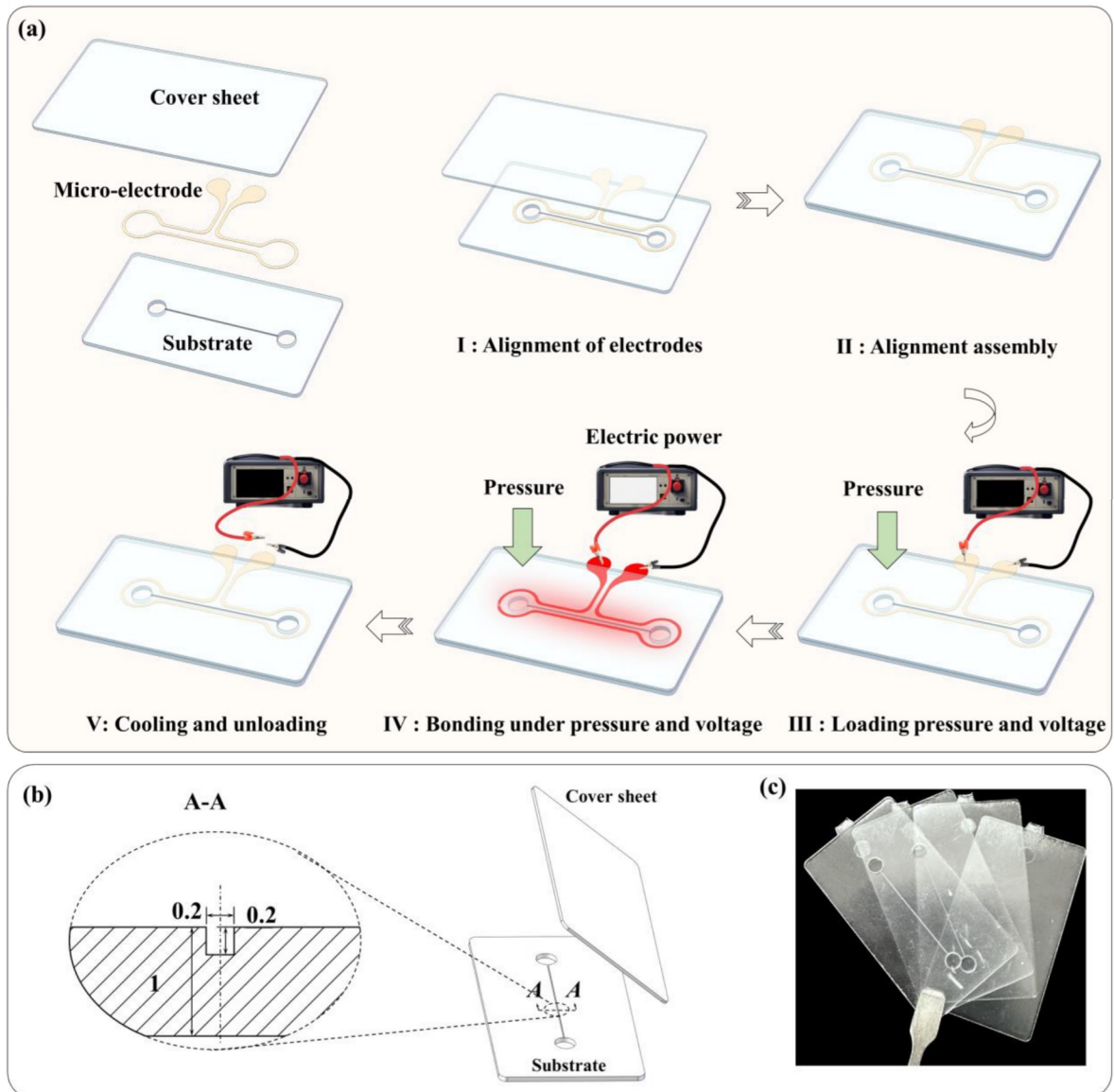
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181 Table 1: The microelectrode bonding parameters.

No.	Voltage (V)	Pressure (kPa)	Time (s)
1	2.5	60	5
2	2.7	90	10
3	2.9	120	15

182

183 To clearly understand how well the microelectrode bonding performance is achieved, an
184 adhesive technology is set as the control. The bonding medium is a polyethylene terephthalate film
185 (PET), which is similar to a double-sided tape (Darit tape, China), with a thickness of 0.01 mm.



186
 187 **Figure 1:** (a) The process flow diagram of the proposed microelectrode bonding process. I: The
 188 microelectrode is placed onto the substrate. II: The cover sheet is placed over the chip and the
 189 microelectrode. III: Pressure and voltage are applied to the assembled chip. IV: The microfluidic chip
 190 gradually reaches temperature over T_m and bonds together under the heat that is generated by the
 191 microelectrodes and the pressure. V: Cooling of the chip back to room temperature via unloading the
 192 bonding voltage, and removing the pressure, to complete the microelectrode bonding process. (b) Schematic
 193 representation of the single-channel microfluidic chip's structure and parameters. The microchannel cross-
 194 section is a 0.2×0.2 mm rectangle. (c) Typical single-channel microfluidic chip that is fabricated by
 195 microinjection molding.
 196

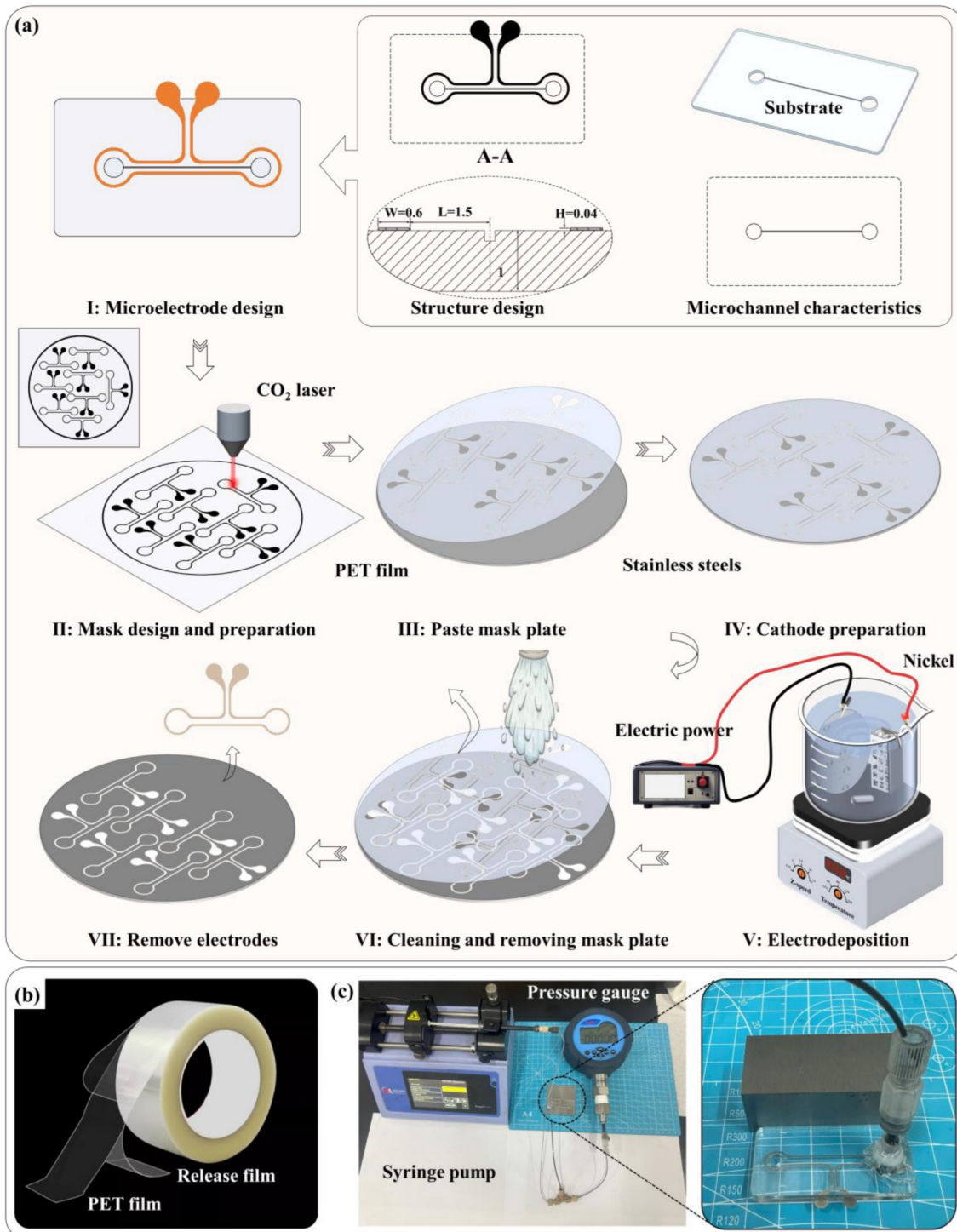
197 **2.3 Microfluidic chip**

198 The aim of this work is to validate and introduce a novel microfluidic chip bonding process;
199 hence, a single-channel microfluidic chip is employed to conduct chip bonding experiments based
200 on microelectrodes. The chip is fabricated through injection molding, with its structure and
201 parameters illustrated in detail in Fig. 1 (b and c). The precision injection molding machine (Arburg
202 370S, Germany) is utilized to produce the single-channel microfluidic chips for bonding. The
203 adopted injection molding parameters are derived from the referenced literature [27,43].

204 **2.4 Electrodeposition**

205 During the bonding process, conformal microelectrodes are used, as illustrated in Fig. 2 (a).
206 First, the microelectrodes are designed based on the microchannels/microstructures of the chip.
207 Their defining structural feature is that the distance between the microelectrodes, as well as both
208 the microchannels and their characteristic structures remain constant. The principle followed is to
209 maintain a constant distance between the microelectrode and the microchannel. The design
210 parameters are microelectrode width, height, and distance from the microchannel. Due to the
211 designed microelectrode dimensions and material characteristics, electrodeposition is employed
212 for the fabrication of the conformal microelectrodes [45–47]. Second, a CO₂ laser is used to
213 engrave PET film as a mask [48–50]. Laser positioning, power and linear speed are critical for
214 precise control of microelectrode manufacturing accuracy. Third, the PET film is glued to a
215 prototype stainless-steel plate. Fourth, insulating the stainless-steel plate. Only the designed
216 microelectrode shape is left exposed. Fifth, connecting the circuit to electrodeposit the

217 microelectrodes. The current density as well as the energization time are also critical for precise
218 microelectrode manufacturing. Sixth, cleaning the cathode and removing the PET mask. At last,
219 finishing the preparation of the microelectrode, via stripping the cathode.



220
 221 **Figure 2:** Schematic diagram of the microelectrode fabrication with an electrodeposition process. (a) I:
 222 Microelectrodes design according to the microchannel/microstructure of the chip. The principle followed
 223 is to maintain a constant distance between the microelectrode and the microchannel. The design parameters
 224 are microelectrode width, height, and distance from the microchannel. II: CO₂ laser engraving PET film as

225 a mask. III: PET film is glued to a prototype stainless steel plate. IV: Insulating the stainless-steel plate.
 226 Only the designed microelectrode shape is left exposed. V: Connecting the circuit to electrodeposit the
 227 microelectrodes. VI: Cleaning the cathode and removing the PET mask. VII: Finishing the preparation of
 228 the microelectrode, via stripping the cathode. (b) The PET film for laser engraving also includes a release
 229 film on both sides. (c) Burst pressure test systems include a syringe pump, a pressure gauge, a syringe, and
 230 connecting pipes. The microfluidic chip is connected to the pipe by adhesive.

231 During electrodeposition, the anode can generate impurities. To prevent these impurities from
 232 entering the electrodeposition solution, an anode bag (containing nickel beads washed with
 233 deionized water) is placed in the anode fixture. A laser engraved mask (high-adhesion PET film)
 234 is adhered to the front side of the stainless-steel cathode plate, while its back and surrounding
 235 edges are sealed with waterproof insulating tape (PVC, Wapodeai 3PCS Electrical Tape). The
 236 microelectrode electrodeposition is carried out using a home-made apparatus (see SFig. 5 in
 237 Supplementary Materials). In this setup, the circuit connections are encapsulated, but the power
 238 supply and cathode plate are connected via alligator clips, as it can be seen in step V of Fig. 2(a).
 239 After electrodeposition completion, the cathode and fixture are separated and rinsed together in
 240 deionized water, followed by drying the electroplated layer's surface with nitrogen. The main
 241 components of the electrolyte and the basic conditions for the electrodeposition experiments are
 242 listed in Table 2.

243 Table 2. The major ingredients of electrolyte and the working condition.

Ingredient of electrolyte ($\text{g} \cdot \text{l}^{-1}$)				Working condition		
Nickel sulphamidate	Nickel chloride	Boric acid	Ethylhexyl sulfate	Temperature ($^{\circ}\text{C}$)	Current density ($\text{A} \cdot \text{dm}^{-2}$)	pH
400	10	30	10	40	0.1, 0.2	3.5–4.5

244 For the electrodeposition experiments, the anode material is nickel of 99.99% purity (VALE
245 INCO, Canada). Before use, the nickel beads are cleaned with deionized water and ethanol, then
246 dried with a nitrogen gun. The electrodeposition cathode is a 304 stainless steel plate with a
247 diameter of 101.6 mm and a thickness of 2 mm, covered with a conformal microelectrode mask,
248 which is prepared by a CO₂ laser engraving machine (YoungLaser V12, Young Chip, China). The
249 mask is a tape of material 0.5 mm thick (polyester film, PET) and serves solely to expose the
250 conformal microelectrode shapes to the electrodeposition solution and electric field, while
251 covering other non-conductive parts of the cathode (see Fig. 2 (b)). The stainless-steel substrate
252 undergoes degreasing and deionization cleaning prior to electrodeposition. The microelectrode
253 electrodeposition experimental conditions are as follows. The electrode gap is 10 cm, the current
254 density is 4 A/dm², and the deposition time is 45 minutes. The power supply equipment used is
255 Agilent B2901A, from Keysight, USA.

256

257 **2.5 Microelectrode and microchannel morphology characterization**

258 For the quantitative characterization of microelectrodes, an Extended Depth of Field
259 Microscopy (KEYENCE®, VHX-5000, Japan) is used as it is capable of capturing clear images
260 across various different depth ranges. By characterizing and comparing the morphology of
261 microchannels before and after bonding, a deeper understanding of the microelectrode bonding
262 process is achieved, promoting its rational application. The deformation of microchannels is
263 assessed by calculating their cross-sectional area. The methodology for this calculation is as

264 described in Equation 1.

$$265 \quad \partial = 1 - \frac{\Delta S_a}{\Delta S_b} \quad (1)$$

266 where ΔS_a is the cross-sectional area of the microchannel after bonding, ΔS_b is the cross-
267 sectional area of the microchannel before bonding.

268

269 **2.6 Bonding strength characterization**

270 The burst pressure of sealed microchannels is used to characterize the bonding strength [51].

271 The bonding strength is precisely measured by monitoring the sudden rupture of the sample under

272 pressure, allowing for direct evaluation of the microfluidic chip bonding performance. This

273 method is selected for its direct reflection of the seal's integrity and quality. The detailed testing

274 apparatus and components are shown in Fig. 2(c), and are primarily comprising of a syringe pump

275 (HARVARD APPARATUS®, HA1100D, USA, flow rate range: 1.28 pl/min - 88 ml/min, liner

276 force: 24 kg, accuracy: 0.5%), a precision pressure gauge with data recording capabilities

277 (ConST211, China, range: 0 - 4 MPa, accuracy: 0.05 - 0.2% full range), and a connecting tube.

278 The bonding strength of the microfluidic chip can be directly read from the pressure gauge. Prior

279 to testing, the adapter must be glued to the cleaned microfluidic chip using epoxy resin adhesive

280 and left to set for 6 hours.

281

282 **2.7 Infrared Imaging**

283 A high-speed infrared camera (ImageIR 8355, InfraTec, Germany) is utilized primarily for
284 observing the uniformity of microelectrode heating and assessing the feasibility of microelectrode
285 application during the microfluidic chip bonding. It is well established that infrared thermal
286 imaging technology plays a crucial role in inspecting heating elements. Therefore, an infrared
287 camera is employed to capture infrared radiation from the surface of microelectrodes and convert
288 it into visualized images of temperature distribution. This approach renders the temperature
289 measurement and monitoring intuitive and contactless.

290 **3 Results and Discussion**

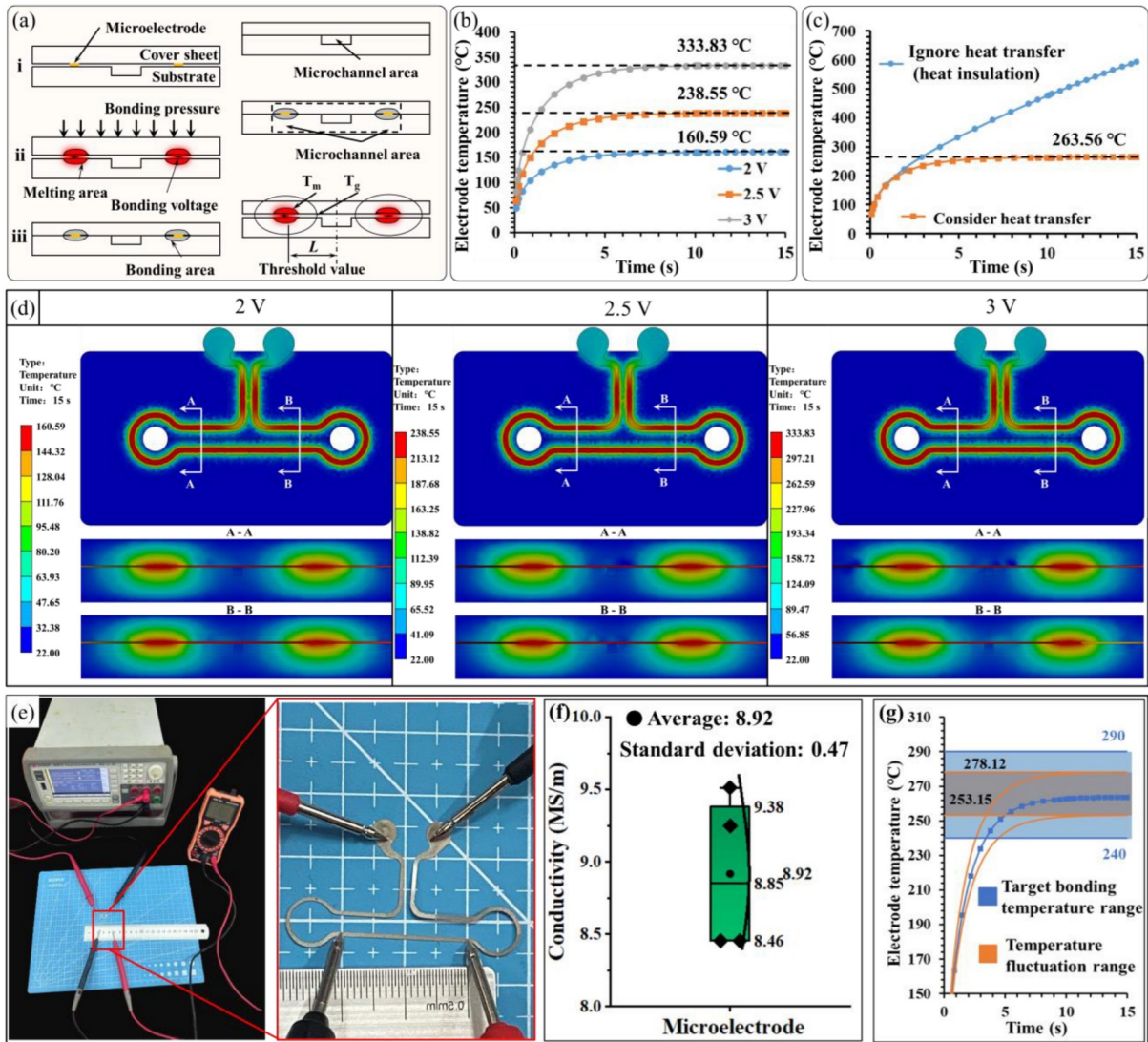
291 **3.1 Influence of microelectrode dimensions and process on bonding**

292 This work proposes a microelectrode bonding technology, which employs the bonding
293 principles and mechanisms that are illustrated in Fig. 3(a). Steps i to iii correspond to the
294 microelectrode bonding process (see Fig. 1(a)). Before performing the microelectrode fabrication
295 and bonding experiments, it is crucial to optimally design the microelectrode dimensions (width,
296 W ; height, H), placement distance (L), and process parameters (bonding voltage, time, and
297 pressure) to optimize bonding quality and process stability (see Figs. 2(a) and 3(a)). Initially, the
298 electrodeposited patterned microelectrodes are not attached to any flexible substrates (e.g., tape or
299 thin film). Therefore, the designed electrodes must possess sufficient mechanical strength to avoid
300 damage (deformation, bending, fracture) during handling or transfer. Microelectrodes that are too

301 narrow or thin increase these risks. However, significant increase to the electrode size is not
302 feasible, as larger dimensions lead to higher resistance, which subsequently increases the bonding
303 energy consumption. While an increase in the width enhances the bonding area and the contact
304 surface of the microchannel, thus improving bonding strength, an increase in height may result in
305 incomplete microchannel sealing. Thus, one of the design principles for microelectrode
306 dimensions is to appropriately increase the width-to-height ratio, while keeping the height at a
307 minimum level to ensure sufficient mechanical strength. Additionally, one advantage of pure
308 electrodes is that they avoid introducing other flexible materials, which could affect microfluidic
309 analysis, such as introducing toxic substances or causing microchannel blockages.

310 Furthermore, the optimization of microelectrode dimensions and the selection of bonding
311 parameters can be precisely determined using finite element analysis simulations. For instance, the
312 impact of in-plane microelectrode morphology on current density and Joule heating is illustrated
313 in SFig. 3 and SFig. 4. The results of this study indicate that the design principle for in-plane
314 microelectrodes is to avoid sharp or right angles in electrodes that are placed on both sides of the
315 microchannel, in order to prevent thermal stress concentration. (For details on the finite element
316 simulation model, material properties, and boundary conditions established based on a 1:1 scale
317 of the chip, see SFigs. 1-4.) The temperature variation of the microelectrode, under different
318 voltage conditions over time is shown in Fig. 3(b). The results prove that under different bonding
319 voltages, the microelectrode reaches and stabilizes at different peak temperatures, rather than a
320 continuous increase over time. The reason is that there is a significant heat exchange taking place

321 between the microelectrode, the microfluidic chip, and the bonding equipment. Evidently, the heat
322 generated and dissipated by the microelectrode reaches an equilibrium. To verify this conclusion,
323 simulations are performed to consider the temperature rise of the microelectrode under both heat
324 transfer and thermal insulation conditions, as shown in Fig. 3(c). The results show that with a
325 bonding voltage of 2.65 V, the microelectrode reaches and stabilizes at a peak temperature of
326 263.56°C after 11 s. Without considering heat transfer (thermal insulation), the microelectrode
327 reaches 593.84°C after 15 s. This showcases that, during microelectrode bonding, the addition of
328 thermal insulation pads can concentrate heat more effectively around the microelectrode, and
329 improve process stability, while avoiding microchannel deformation caused by excessive
330 temperatures. In parallel, one can understand that the phenomenon of peak temperature at different
331 voltages is critical for the stability of the proposed microelectrode bonding process. This indicates
332 that when the uniformity of microelectrode dimensions is adequately supported by mass
333 production technologies, microelectrodes will be able to stably bond microfluidic chips at a fixed
334 bonding voltage. Therefore, the precise control of microelectrode bonding temperature through the
335 control of bonding voltage is one of the advantages of this technology. Subsequently, it is proven
336 that the microelectrode bonding process exhibits stable characteristics, with the stability of
337 bonding quality depending primarily on the fabrication precision of the microelectrode dimensions.



338
 339 **Figure 3.** (a) Schematic diagram of the microelectrode bonding mechanism. (b) Graph showing the temperature
 340 variation of the microelectrode, under different voltage conditions over time. (c) Graph showing the temperature
 341 rises of the microelectrode, under both heat transfer, and thermal insulation conditions. (d) The distribution of
 342 temperature curves near the microelectrode and the microchannel under different bonding voltages. (e) The four-
 343 point probe method used to accurately measure the electrical conductivity of the samples. (f) The electrical
 344 conductivity of the four microelectrodes and its distribution. The fluctuation range of the conductivity is less
 345 than 5.29% of the mean value. (g) Graph showing the electron temperature versus time. Notice that the range of
 346 maximum temperature variation in the microelectrodes caused by conductivity fluctuations remains within the
 347 ideal bonding temperature range.

348 After determining the basic dimensions of the microelectrode, the bonding parameters are set
 349 based on two factors. Bonding voltage, which is determined by the temperature at which the

350 microelectrode reaches its peak, and the bonding time, which is determined by the time period
351 required for the microelectrode temperature to stabilize. The microelectrode temperature is set
352 according to the melting temperature of the microfluidic chip material. In this case, the injection
353 molding temperature range for PMMA is 240 - 290°C, therefore the optimal bonding temperature
354 is selected within this range. Temperatures below this range result in incomplete bonding and low
355 bonding strength, while exceeding this range leads to polymer thermal decomposition and
356 significant deformation or blockage of the microchannel. Bonding time appears to invoke similar
357 effects. A bonding time that is too short prevents the microelectrode from reaching its peak
358 temperature, reducing bonding strength and process stability, while excessive bonding time
359 decreases bonding efficiency.

360 The appropriate design of the distance between the microelectrode and the microchannel is
361 essential for the precise control of the microchannel height. When this distance is below the
362 threshold, even a low bonding pressure can cause significant microchannel deformation due to
363 excessively high temperatures around the microchannel. Only when the microelectrode position
364 exceeds the threshold will the impact of bonding temperature be minimized. Thus, the design
365 principle for the microelectrode position threshold is that when the microelectrode temperature
366 reaches or exceeds the polymer's melting temperature, the temperature near the microchannel must
367 remain below its glass transition temperature to avoid significant deformation. The definition of
368 this threshold can be found in Fig. 3(a). Fig. 3(d) displays the distribution of temperature curves
369 near the microelectrode and microchannel under different bonding voltages, which serves as an

370 important reference for the determination of the microchannel placement distance. Accordingly,
371 hugely increasing the microelectrode placement distance enlarges the in-plane microchannel area
372 (see Fig. 3(a)), and, thereby, the size of the microfluidic chip. This threshold is also influenced by
373 parameters such as microelectrode material (resistance, conductivity), cross-sectional area, length,
374 and bonding voltage. Therefore, conducting finite element simulations during the microelectrode
375 bonding design phase is necessary to optimize these parameters.

376 The electrical conductivity of the electrodeposited nickel electrodes also plays a crucial role
377 in determining the efficiency and uniformity of the Joule heating process. In this work, the
378 electrical conductivity of the nickel electrodes is measured to ensure consistency, and to evaluate
379 the potential impact on scaling up the bonding process. The four-point probe method is employed
380 to accurately determine the electrical conductivity (σ) of the sample. This method, known for
381 minimizing contact resistance effects, is adapted to account for the microelectrodes. The power
382 supply described in Section 2.4 is used to provide a stable 1 A direct current (I) for the experiments.
383 The four probes are arranged as shown in Fig. 3(e). A known current is applied through the two
384 outer probes, and the voltage drop (V) is measured across the two inner probes. The distance
385 between the electrodes is denoted as L . The electrical conductivity is calculated using the equation
386 $\sigma=(L \cdot I) / (V \cdot A)$, where A is the cross-sectional area of the microelectrodes. The conductivity
387 measurements performed for the four microelectrodes are shown in Fig. 3(f), having a fluctuation
388 range of 5.29%. Based on this fluctuation range, follow up simulations assess the effect of
389 electrical conductivity on the maximum temperature of the microelectrodes under identical process

390 conditions, as illustrated in Fig. 3(g). The temperature fluctuation range caused by variations in
391 electrical conductivity is found to be 253 - 278°C, which is within the ideal bonding temperature
392 range (240 - 290°C). One can see that while the microelectrode bonding process allows for precise
393 temperature control, the bonding stability is dependent on the consistency of the microelectrode
394 fabrication process and the stability of its electrical conductivity. The study results demonstrate
395 that the fluctuation in the maximum heating temperature, caused by differences in the electrical
396 conductivity of electrodeposited microelectrodes, remains within the ideal bonding temperature
397 range. This finding establishes a theoretical foundation for achieving efficient and stable
398 microelectrode bonding and provides a crucial basis for optimizing their performance.

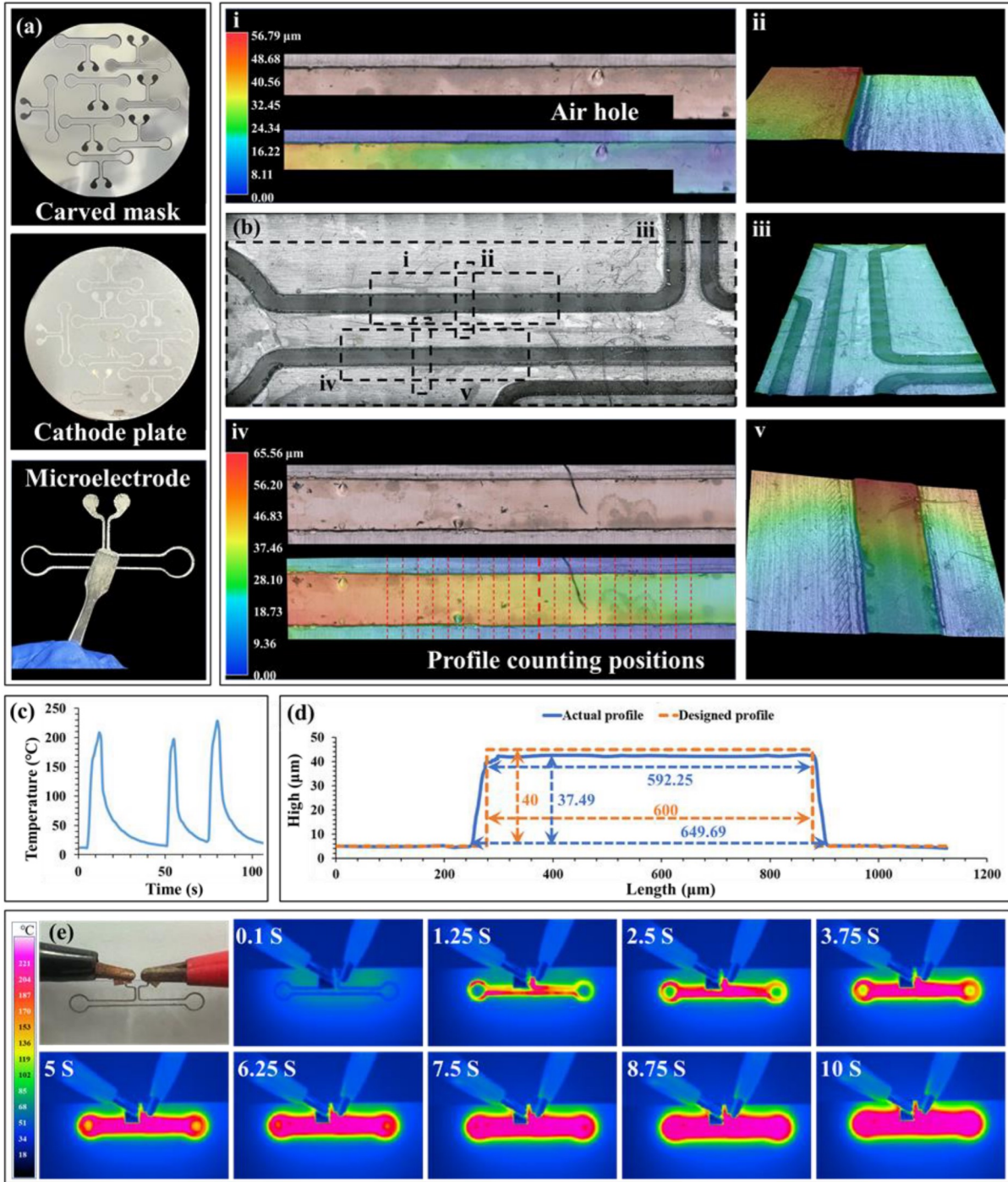
399 The bonding pressure is the last factor to be considered. Based on the schematic of the
400 microelectrode bonding process (see Fig. 3(a)) and the stability analysis of microelectrode
401 temperature, once the microelectrode temperature and position are determined, the only process
402 parameter affecting the microchannel height is the bonding pressure. Therefore, when the polymer
403 surrounding the microelectrode reaches its melting temperature, applying an appropriate bonding
404 pressure is sufficient to seal the microchannel. Increased bonding pressure is the direct cause of
405 microchannel deformation. Thus, precisely controlling the bonding pressure uniformly and
406 keeping it as low as possible during microchannel sealing is crucial for accurately controlling the
407 microchannel height. Additionally, compared to thermal bonding and ultrasonic welding, the lower
408 bonding pressure (by 1-2 orders of magnitude) is a distinct advantage of microelectrode bonding
409 technology.

410 **3.2 Microelectrode morphology and heating**

411 The physical form and surface characteristics of microelectrodes significantly impact their
412 performance, particularly in heat generation and conduction for applications such as polymer
413 melting during the microfluidic chip bonding processes. Fig. 4(a) shows the PET mask, cathode,
414 and electrodeposited microelectrode, respectively. The mask plate is quickly and easily prepared
415 (40 s) with the laser engraving equipment, aided by computer assisted design, to enable rapid
416 iteration of the microelectrode structure. Subsequently, the microelectrodes are separated intact
417 from the stainless-steel cathode. This demonstrates that the electrodeposition process can be
418 adapted to microelectrode processing. It is important to note that the precision in microelectrode
419 manufacturing determines their dimensional accuracy, which in turn influences their heating
420 uniformity. The latter is an essential factor for the reliable microfluidic device operation.
421 Consequently, Fig. 4(b) elucidates the morphology of microelectrodes prepared by
422 electrodeposition. The results indicate a deviation between the microelectrodes that are prepared
423 by laser-engraved masking followed by electrodeposition and their designed dimensions. The
424 cross-sectional profile of the microelectrodes, averaged over 20 profile lines, appears as a trapezoid
425 as depicted in Fig. 4(d), with base, top, and height dimensions of 649.69 μm , 592.25 μm , and 37.49
426 μm respectively. The deviation springs from the enlargement of dimensions that are caused by the
427 laser heat, which is scorching during the mask engraving process. This error is typically eliminated
428 by adjusting the laser intensity or the design dimensions. Similarly, thickness deviation is rectified
429 by modifying the electrodeposition duration. However, when used as heating elements, the surface

430 flatness and uniformity of the microelectrodes are of paramount importance. This is due to the fact
431 that only microelectrodes with consistent physical characteristics ensure uniform heating effects.
432 Any sudden changes in local dimensions result in rapid or slow temperature changes, causing
433 uneven bonding, which typically manifests as scorching or leaks in the final fabricated
434 microfluidic chips. Despite dimensional inaccuracies and micro-pits on the surface, the overall
435 shape of the microelectrode is regular and intact. Consequently, these electrodes are appropriate to
436 be used for microfluidic chip bonding. Evidently, electrodeposition is affirmed as an ideal process
437 for preparing this type of microelectrodes.

438



439

440 **Figure 4:** The structure, morphology and heating properties of electrodeposited microelectrodes. (a) The
 441 PET mask, cathode, and electrodeposited microelectrode. (b) The surface morphology of electrodeposited
 442 microelectrode. (i-v) The 3D morphology of different regional locations. Notice that the overall uniform
 443 structure is able to meet the bonding requirements, with the exception of a few holes. (c) Temperature
 444 profile of multiple heating of the microelectrode in air at bonding voltage of 3V. (d) Differences between

445 microelectrode profiles (averaged from 20 profiles, positions referenced to (b) (iv)) and design profiles. It
446 is important to note that machining errors are within acceptable limits. (e) Microelectrode heating
447 uniformity is characterized by infrared thermography at a 3V bonding voltage. Notice that after 4 seconds,
448 there is a uniform microelectrode heat distribution.

449

450 The heating rate is the initial focus in the discussion of the microelectrode heating
451 performance. The material for this specific microelectrode is nickel, an excellent thermal
452 conductor, which efficiently converts electrical energy into heat. The heating rate of the
453 microelectrode, as well as the temperature rise curve at ambient temperature with an applied
454 voltage of 3 V, are depicted in Fig. 4(c). The test results showcase a heating rate that ranges
455 between 40-80 °C/s, showcasing that it allows for PMMA to achieve the T_m rapidly. As
456 documented in literature [27], T_m of PMMA CM-205 is about 240°C. This rapid heating renders
457 microelectrode bonding technology advantageous comparing to others in literature, as it enables
458 rapid high-strength thermal fusion in solely a few seconds. Theoretically, the microfluidic chips
459 can be heated to the molten state within approximately 3-6 seconds. However, further increasing
460 the heating rate may lead to issues such as polymer volatilization. Extending the bonding time
461 marginally helps optimize these issues based on the observed heat transfer between the chip and
462 the pressure apparatus during pressure application. To elucidate the mechanism and calculate the
463 real required voltage and time, one must determine them through additional experiments.

464 Fig. 4(e) shows a series of infrared thermal images that are depicting the heating of
465 microelectrodes. Due to their 40 μm thickness, the microelectrodes are prone to warping and
466 deformation in air. As previously mentioned, this is caused by the rapid heating and stress

467 concentration during the heating process. To circumvent this issue, the microelectrodes must be
468 clamped between two glass slides. However, infrared is absorbed or reflected when passing
469 through glass, which means that infrared images taken through glass may not accurately depict the
470 reality. This approach is appropriate as the aim is to analyze the microelectrode heating uniformity,
471 and the precise temperature rise curve of the microelectrode is already demonstrated in Fig. 4(c).
472 It needs to be clarified that, therefore, the provided temperature scale in Fig. 4(e) is for reference.
473 Nonetheless, the images reveal that heat is primarily concentrated in the areas where the electrodes
474 connect. In terms of heat distribution uniformity, infrared imaging in the first 3 seconds clearly
475 shows variations, with the central part of the electrode heating faster than its ends. Over time, the
476 heat disperses across the entire electrode, achieving a relatively uniform distribution after 4
477 seconds of power application. This is attributed to geometric factors (uniform contact (guaranteed
478 by bonding pressure), and electrode size) affecting heat conduction. Following this
479 characterization, the researchers suggest that for microfluidic chip bonding applications, the
480 voltage should be lowered and the duration extended. Regarding, other applications that might
481 require a more detailed and in depth understanding of the thermodynamics, as well as the ones that
482 have less margin of tolerance, further experimental analysis is required in order to achieve more
483 precise and controlled microfluidic chip bonding.

484 **3.3 Bonding performance**

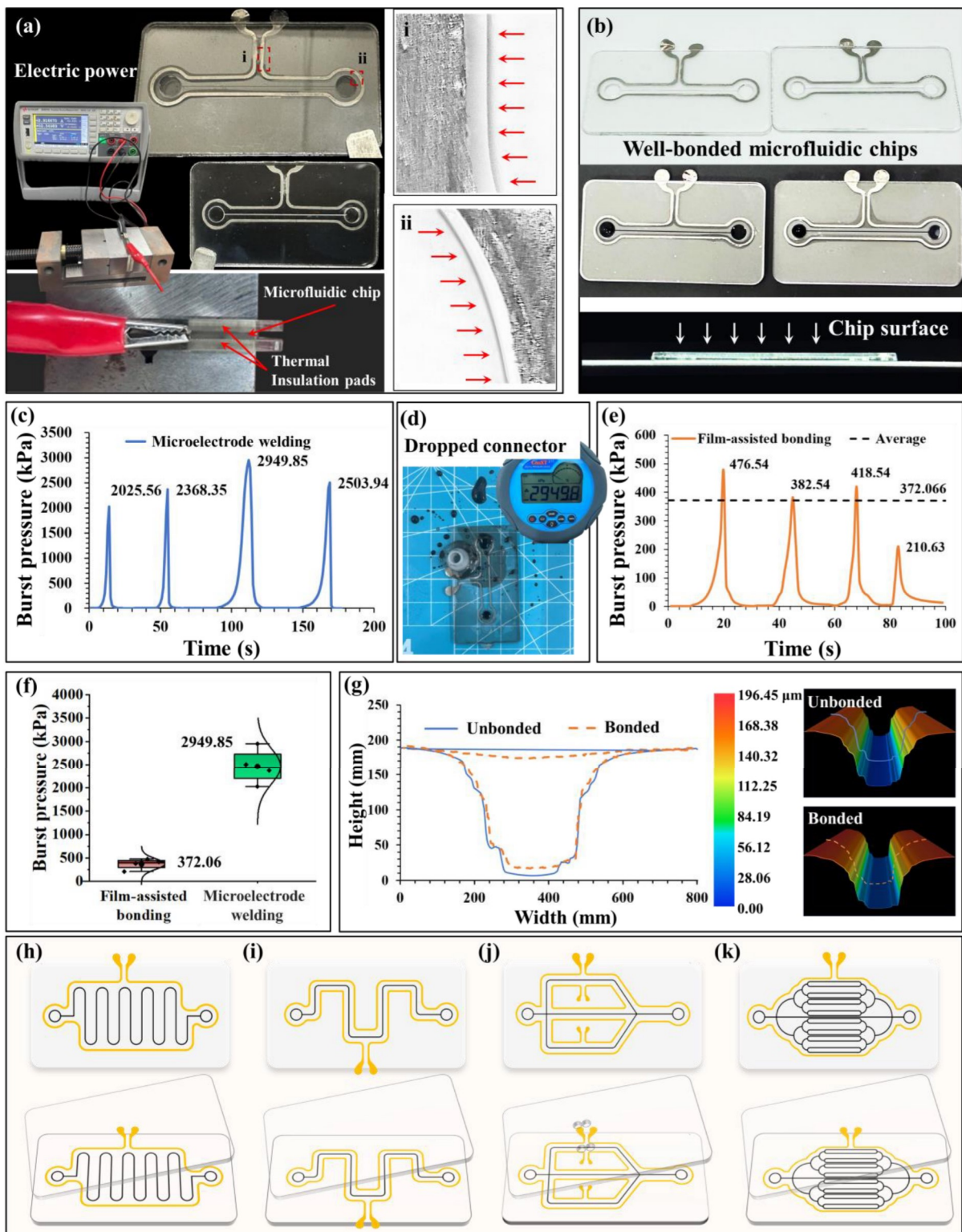
485 This section presents the microelectrode bonding experiments conducted on the microfluidic
486 chip. The microelectrode-based microfluidic chip bonding process is simple and only uses a power

487 supply and a small vise (see Fig 5(a)). The results demonstrate that when a 3 V voltage and a 10 s
488 bonding time are applied, one can observe significant bonding traces around the microelectrodes.
489 The microelectrodes, upon heating, allowed the surrounding areas of the microfluidic chip to have
490 temperatures over the T_m , leaving behind bonding traces as can be seen in Fig. 5(a). This clearly
491 evidences the feasibility of the microelectrode bonding process. The bonding traces that appear on
492 both sides of the microelectrodes showcase that the microfluidic chip is heated to the molten state,
493 and is subsequently merging the cover sheet and the substrate together. Simultaneously, a certain
494 distance between the named bonding traces and the microchannels still remains. This suggests that
495 the molten polymer does not flow through, and does not result in the blocking of the microchannels.
496 Therefore, as long as the distance between the microelectrodes and the microstructures is
497 controlled, it effectively mitigates or avoids completely any creation of the microstructure
498 deformations.

499 Considering the optimization of the proposed bonding process (as well as any other bonding
500 process), it needs to be in alignment with applications, whereas the bonding strength of the
501 microfluidic chip and the morphology of the microchannels are comprehensively considered.
502 Results from bonding experiments reveal that when the voltage is below 2.5 V, the microfluidic
503 chip seal unsuccessfully within the 15 seconds, although bonding traces can still be identified. The
504 primary reason lies in the fact that the microelectrodes are not capable of generating the sufficient
505 amount of heat that is required to reach the T_m of the polymer, with a 2.5 V voltage. Additionally,
506 the significant heat conduction that exists between the chip and the holding vice is also a factor

507 that results in the above-mentioned phenomenon. Several measures are implemented to address
508 these issues. The voltage is increased to 2.7-2.8 V, and there is an implementation and usage of
509 thermal insulation pads to allow for a well-bonded chip (see Fig. 5(b)). In this work, the
510 microelectrode has a thickness of 0.04 mm, which is 1/45th the thickness of the microfluidic chip
511 (1.8 mm). The impact of the microelectrode thickness is negligible, even when it reaches the
512 polymer's melting temperature (see SFig. 6). Uniform heat generation, coupled with the parallel
513 application of bonding pressure, ensures that the microelectrode remains free from warping or
514 deformation. This is further corroborated by the bonding experiments shown in Figs 5(a) and (b),
515 which demonstrate that there is no evidence of deformation. In reality, uniform thermal cycling
516 helps to relieve residual stress in the chip, ultimately improving its flatness. The bonded
517 microchannel successfully facilitates capillary-driven flow of the indicator liquid (shown in Fig.
518 5(b)). Furthermore, high-resolution microscopy of the reconstructed microchannel morphology (as
519 seen in Fig. 5(g)) appears to have no evidence of channel closure. Fig. 5(c) shows the burst pressure
520 profiles of four samples, when the bonding process parameters are 2.8 V, 60 kPa, and 15 s. The
521 results indicate that when employing the microelectrode bonding technology, the bonding strength
522 of the chip exceeds 2.9 MPa, as the chip did not separate as initially predicted and anticipated at
523 this value. During the testing process, the chip joints that are bonded by epoxy resin adhesive are
524 the first to detach from the chip due to the applied pressure (Fig. 5(d)). This shows clearly and
525 provides evidence that within the testing system, the adhesive-bonded connectors are the weakest
526 points in terms of strength. From this experiment, we can logically claim that the strength achieved

527 with the proposed bonding process is larger than 2.9 MPa.



528

529 **Figure 5:** Microelectrode bonding performance of microfluidic chips. (a) The microelectrode bonding
530 apparatus, which requires only an electrical power supply and a small vise. (i-ii) Examples of microscope
531 images that show bonding traces observed at different positions. (b) Photos of the well-bonded microfluidic
532 chips. (c) Graph of burst pressure versus time, showing the burst pressure curve for 4 different chips that
533 bonded at 2.8 V and 60 kPa with 15 s. (d) Photo of the adhesive connector used, as it fails during the burst
534 pressure test, showcasing that the chip's bond strength is greater than 2.9 MPa. (e) Plots of burst pressure
535 versus time for the same four burst pressure curves of the chips that are bonded with PET film. (f) Graph
536 of burst pressure versus time, comparing the microelectrode bonding with film-assisted bonding, where the
537 former exhibits higher burst pressure than the latter. (g) Plots and graphs of microchannel profiles before
538 and after microelectrode bonding. The results show that microelectrode-bonded microchannel deformation
539 is less than 10% comparing to pre-bonding. (h) Schematic of microelectrode bonding schemes that can be
540 adopted for dense serpentine microchannels. (i) Schematic of the high sealing requirements of serpentine
541 microchannels. These can be addressed by increasing the chip bonding area as seen here. (j) Schematic
542 showing the sealing of annular microchannels. This places new demands on the bonding scheme. (k)
543 Schematic representation of dense mesh microchannels, showing that the suitability of microelectrode
544 bonding depends on the application requirements. Microelectrode bonding still shows advantages in most
545 application cases.

546 For direct comparison, adhesive bonding technology is used to bond the same microfluidic
547 chips. The continuous burst test curves for four samples are plotted in Fig. 5(e). The test results
548 clearly evidence that with increasing test pressure, leakage phenomena consistently occur at the
549 bonding interfaces of the test samples. The average bonding strength of adhesive bonding is 372.06
550 kPa, which is significantly lower than the microelectrode bonding strength of 2949.85 kPa (see
551 Fig. 5(f)). This provides a considerable advantage in bonding strength for the microelectrode
552 bonding. Regarding the bonding strength formation mechanism, the adhesive bonding or the film-
553 assisted bonding primarily rely on the bonding of molecular chains that provide the necessary
554 bonding strength. Microelectrode bonding on the other hand achieves bonding by using a
555 mechanism of heating the microfluidic chips to T_m , followed by merging and cooling, via
556 integrating the cover and base substrates into one. Theoretically, microelectrode bonding can

557 enhance the bonding strength of the chips to reach the inherent strength of the material itself. In
558 the examined current case, it is indeed proven that the strength derived from microelectrode
559 bonding considerably exceeds the one that is obtained through interlocking molecular chains or
560 chemical bonds.

561 Microchannel deformation is also a critical process parameter, since it significantly influences
562 both the chip performance, as well as its intended function. The microchannel morphology before
563 and after bonding, along with the microchannel deformation, are depicted in Fig. 5(g). The results
564 reveal a microchannel deformation of 9.9%. The minor deformation is characterized by the
565 depression of the cover piece as well as the decreasing microchannel height. This indicates that
566 the rapidly generated heat is relatively concentrated near the microelectrode without causing a
567 sudden temperature rise in the microchannel. On the other hand, it also shows that the 60 kPa
568 pressure satisfies the bonding requirements without causing significant deformation. According to
569 current literature, the state-of-the art for a microchannel deformation rate is 15% with a bonding
570 strength of 0.64 MPa under the process parameter combination (pressure: 0.35MPa) using thermal
571 bonding technology [27].

572 To summarize the above findings, the current study has shown that the proposed
573 microelectrode bonding achieves lower microchannel deformation (9.9%) and higher bonding
574 strength (>2.9 MPa), while using lower pressure (0.06 MPa). Additionally, microelectrode bonding
575 does not necessitate the use of complex equipment. One can therefore conclude that the innovative
576 process design of using microelectrodes for microfluidic chip bonding exhibits significant

577 advantages over the traditional bonding methodologies. Finally, it should be emphasized that the
578 microelectrode bonding method, in its current form, is optimized for thermoplastic polymer-based
579 materials (in this case PMMA). The authors expect that direct bonding of non-polymeric materials,
580 as for example silicon, silicon oxides, silicon nitrides, and silicon carbides, is not feasible without
581 severe method modifications.

582

583 **3.4 Advantages and limitations of microelectrode bonding comparing with literature**

584 The discussion regarding the advantages of microelectrode bonding, revolves around
585 efficiency, performance, cost, equipment complexity, and safety aspects. Table 3 summarizes the
586 literature in bonding performance of microfluidic devices that use thermoplastic materials over the
587 last ten years. Starting with efficiency, in comparison with thermal bonding and solvent bonding,
588 which can take several minutes to tens of minutes, microelectrode bonding demonstrates a clear
589 advantage, with times spanning to the regions of tens of seconds (in this case less than 15s). Other
590 processes include laser and ultrasonic welding. Even when considering the preparation time for
591 microelectrodes, microelectrode bonding technology can still be holding the potential for further
592 efficiency improvements. While ultrasonic welding (UW) is indeed suitable for large-scale
593 manufacturing, the proposed microelectrode bonding offers unique advantages. These are the
594 precise heat control, the lower energy consumption, and the cost-effectiveness in combination with
595 minimal equipment requirements. In MB, the heat is generated through localized Joule heating of
596 the microelectrodes, allowing the precise control of the temperature distribution and the heating

597 duration (detailed in Section 3.1). Contrarily, UW relies on mechanical vibrations to generate heat,
598 which leads to poor control of temperatures, subsequent warping or distortion, especially in the
599 case of smaller microfluidic structures. Moreover, the parameter combination of ultrasonic
600 welding, needs to be obtained through a lot of basic experiments. As evidenced in previous
601 chapters, MB operates at low voltages (2.5-2.9 V) and requires significantly less energy than UW,
602 which needs high-frequency vibrations and substantial power input. Moreover, MB only requires
603 a simple power supply and a bench vice to apply pressure, which is much less complex than UW
604 systems that require high-frequency vibration generators and acoustic tools. Additionally, the
605 presence of the energy-gathering rib structure further increases the processing difficulty, time, and
606 cost for fabricating the chip or mold. These features make microelectrode bonding a promising
607 approach for applications where precision and minimal deformation are essential.

608 For thermoplastic microfluidic chips with commercial potential, plasma treatment is typically
609 introduced as an auxiliary or pre-treatment step, during thermal compression bonding processes.
610 As emphasized in the introduction, the combination of multiple techniques inevitably adds to the
611 complexity of a bonding process, not only with additional steps, but also introducing expensive
612 and complex (e.g. low-vacuum) equipment. This is precisely the motivation behind proposing the
613 microelectrode bonding process, which aims to enhance bonding performance while simplifying
614 the process and conditions, and reducing the need for specialized equipment. In summary, even
615 though plasma-activated bonding has profound advantages, i.e. such as room-temperature bonding
616 and minimal thermal input, the microelectrode bonding technique offers the distinct innovations,

617 including of precise thermal control, environmental friendliness, high bonding strength, material
618 versatility, and simplified equipment requirements.

619 Due to the additional microelectrode production steps introduced by MB technology, the
620 method seems limited in mass production. However, a potential expansion of the cathode plate
621 area in combination with an increasing current density, can lead to a significant enhancement of
622 the fabrication efficiency of single electrode. Moreover, batch fabrication technology, as for
623 example screen printing and 3D printing have the clear potential to further increase production
624 efficiency and reduce bonding costs. With these the single electrode production time can go down
625 to a few minutes, allowing for the lowering also of production costs [52–55]. On the other hand,
626 MB technology has further development potential. For instance, integrating MB into molds
627 (similar to in-mold thermal compression bonding) can offset the limitations brought by additional
628 production steps (see SFig. 7). It is important to emphasize that although this work is not yet
629 complete, the authors are confident that it will be a significant direction for future research. This
630 process only requires minor modifications to the molds, thus simplifying the production process
631 of microfluidic chips by eliminating cleaning and drying steps. However, ultrasound, laser systems,
632 or solvent bonding technology are not suitable for in-mold applications due to the constraints of
633 mold size or bonding efficiency. Furthermore, the overall advantages of MB in terms of bonding
634 efficiency, devices, performances, and operational efficiency are sufficient to offset the impact
635 caused by the microelectrode processing steps.

636 Considering all the above and to the best of the authors' knowledge, the performance of the

637 above described microelectrode bonding method, which shows burst pressures higher than 2.9
638 MPa and microchannel deformation rates less than 10% is the best recorded so far in the literature
639 of bonding technologies. When it comes to burst pressure, it may vary with the microchannel
640 structure and dimensions, i.e., the bonding strength decreases when using a complex microchannel
641 for testing. However, the microchannels tested in this study are similar in structure and dimensions
642 to those reported in most references. Therefore, the burst pressure of 2.9 MPa, used as comparative
643 data, has objective confidence and reference value. Additionally, it should be noted that the
644 microelectrode bonding does not require complex additional devices. A controllable power supply
645 and a vice are sufficient to complete chip bonding immediately. Simultaneously, unlike laser
646 methods, which require absorptive materials or the addition of absorbers, microelectrode bonding
647 is suitable for bonding using most of the amorphous transparent materials, corresponding to the
648 ability of the method to avoid impact on optical analyses. Similarly, unlike solvent bonding and
649 film-assisted bonding, which require the introduction of volatile solvents (acetone, isopropanol)
650 and interlayers, microelectrode bonding does not introduce any impurities or chemical reagents,
651 ensuring absolute safety. There are no stringent requirements for the raw materials in
652 microelectrode bonding. Theoretically, any conductive material such as platinum, copper, iron, and
653 carbon fiber can be used to fabricate microelectrodes.

654

655 Table 3: Differences between microfluidic chip bonding methods for common thermoplastic materials in terms
656 of process, burst strength, and efficiency.

Method	Material	Effective Parameters	Burst pressure	Published Years	Supplementary	Ref.
Plasma treatment + Surface modification	PDMS-PMMA	Bonding time: 40 min.	622 kPa	2022	/	[56]
Solvent-assisted thermal bonding	PMMA-PMMA	Bonding time: 40 min. Bonding temperature: 70°C. Bonding pressure: 10 kPa.	1000 kPa	2022	Multilayer bonding Propan-2-ol, (IPA, [57] poisonous) 60 vol%	
Solvent Vapor-assisted thermal bonding	COC-COC	Bonding time: 16 min. Bonding temperature: 72°C. Bonding pressure: 3993 – 7985 N.	1700 kPa	2022	cyclohexane and 40 vol% acetone (poisonous). [58]	
Film-assisted thermal bonding	PMMA-TPE, PMMA-PMMA	Bonding time: 15 min. Bonding temperature: 84°C (PMMA), 70°C (TPE). Bonding pressure: 2.4 MPa (PMMA), 1.6 MPa (TPE).	1000 kPa	2021	/	[59]
Intermediate bonding	PDMS-PMMA	Bonding time: 60 min.	436.65 kPa	2019	Sputter-coated silicon dioxide + oxygen plasma Polyethylene	[60]
Film-assisted thermal bonding	PMMA-film-PMMA	Bonding time: 10 min.	Over 2 MPa	2018	terephthalate + UV curing adhesive [61]	
Solvent-assisted thermal bonding	PMMA-PMMA	Bonding time: 20 min. Bonding temperature: 60°C.	655 kPa	2017	/	[62]
Solvent-assisted thermal bonding	PMMA-PMMA	Bonding time: 15 min. Bonding temperature: 68°C.	660 kPa	2016	Isopropyl alcohol (poisonous) [63]	
Adhesive bonding	PMMA-PDMS	Bonding time: ~5 min. Bonding time: 30 min.	345 kPa	2021	Biocompatible adhesive tape + oxygen plasma treatment [64]	
Solvent bonding	PLA-PMMA	UV light. Annealing temperature: 50°C	1.352 MPa	2018	/	[25]
Thermal bonding	PMMA-PMMA	Bonding time: 5 min. Bonding temperature: 103°C. Bonding pressure: 0.3 MPa	600 kPa	2023	Highly dynamic tempered in-mold thermocompression [27,6 5]	

		bonding			
Thermal bonding	PMMA-PMMA	Bonding time: 5 min. Bonding temperature: 109°C. Bonding pressure: 1.7 MPa	1.77 MPa	2023	Structural design [43]
Microelectrode bonding	PMMA-PMMA	Bonding time: 15 s. Bonding voltage: 2.8 V. Bonding pressure: 60 kPa.	Over 2.9 MPa	This work	This work

657 Nonetheless, there are some limitations for the microelectrode bonding. The microelectrode
658 bonding strategy differs depending on the application, particularly for denser serpentine
659 microchannels. When there is no need to consider fluid exchange between channels, the perimeter
660 can be sealed as shown in Fig. 5(h). Conversely, when stringent control of internal pressure and
661 fluid flow rate in the channels is necessary, microchannels may be fully surrounded (see Fig. 5(i)),
662 though this vastly increases the space that is occupied by the microchannel (see Fig. 3). In cases
663 where the surface area of the microfluidic chip is strictly limited, the viability of the microelectrode
664 bonding process will depend on the sealing integrity between the microchannels and the specific
665 application requirements. It is important to note that ultrasonic and laser welding also face similar
666 challenges, as they require a number of considerations of the laser path and energy-gathering ribs,
667 respectively. This showcases that those chips that are suitable for laser or ultrasonic welding are
668 also amenable to microelectrode bonding, which suggests that the advantages of these methods
669 have subsequently become quite limited. There is also the chance that microelectrode bonding may
670 not be applicable to microfluidic chips with dense microchannel networks and strict fluid control
671 requirements (Fig. 5(k)), since it depends on the requirements of specific application. For the case
672 of the serpentine microchannels (see 5(j)), higher demands are placed on microelectrode

673 fabrication precision, as well as the bonding power source, and the microfluidic chip area. One can
674 clearly see that the microelectrode bonding shares similar application scopes with ultrasonic and
675 laser welding. However, for large storage pools or arrayed micro-structures, microelectrode
676 bonding is more advantageous than thermal compression bonding, which causes significant
677 deformation. Finally, possibly the most substantial challenge faced by microelectrode bonding is
678 the rapid increase in microchannel area. Whether the method is suited for chips with dense
679 networked microchannels, needs to be further and carefully examined to clarify the handling of
680 the appropriate fluid control requirements. For most applications of dense microchannel network,
681 we consider the external enclosure method shown in Fig. 5(k) to be feasible.

682 **4 Conclusions and prospects**

683 The development and commercialization of microfluidic chips have been hindered by the
684 limitations of existing bonding technology, which often result in inadequate bond strength and
685 significant deformation. This study introduces a novel microelectrode bonding technology for
686 microfluidic chips, addressing the critical need for reliable, cost-effective, and high-throughput
687 bonding methods in microfluidic technology. Specially, the bonding or sealing mechanism can be
688 controlled by the applied voltage and duration, i.e., the microelectrode bonding technology.

689 Our electrodeposition method, utilizing a nickel sulphamidate-based electrolyte and CO₂
690 laser-engraved PET masks, allowed for the rapid production of microelectrodes precise dimensions
691 (base: 649.69 μm, top: 592.25 μm, height: 37.49 μm). These electrodes demonstrated excellent

692 heating performance, achieving rates of 40-80 °C/s at 3V, enabling rapid polymer melting for
693 bonding. Our research demonstrates that the microelectrode bonding process achieves substantial
694 bonding strength with minimal deformation. Specifically, applying a voltage of 2.8V, a pressure of
695 60 kPa, and time of 15s results in bond strengths exceeding 2.9 MPa. This method marks a
696 substantial improvement over traditional adhesive bonding technology, which exhibit average
697 bond strengths around 372.06 kPa. Additionally, the process ensures minimal deformation due to
698 the rapid and controlled heat generation at the bonding interface.

699 Unquestionably, despite the previously analyzed results, there is a necessity for further
700 research that arises, in order to investigate this technique across the spectrum of the polymeric
701 materials and the microfluidic designs. Since this is a microfluidic product, it is also necessary to
702 investigate long-term stability under various operational conditions. For this study to reach its
703 potential in impact, future studies need to explore the scalability of this method for high-throughput
704 manufacturing.

705 Evidently, the microelectrode bonding technology significantly advances the field of
706 microfluidic chip fabrication, offering a pathway to more reliable and efficient devices that can
707 meet the demands of commercial and research applications.

708 **CRedit authorship contribution statement**

709 **Baishun Zhao:** Conceptualization, Investigation, Writing – Original Draft, Writing - Review &
710 Editing, **Wangqing Wu:** Conceptualization, Writing – Review & Editing., Funding acquisition,

711 Resources. **Dimitrios Kontziampasis**: Writing - Review & Editing. **Lei Huang**: Data curation.
712 **Bingyan Jiang**: Project administration, Funding acquisition, Resources.

713 **Declaration of competing interest**

714 The authors declare that they have no known competing financial interests or personal
715 relationships that could have appeared to influence the work reported in this paper.

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723 **Data availability**

724 All data included in this study are available upon request by contact with the corresponding
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726 **References**

- 727 [1] E.K. Sackmann, A.L. Fulton, D.J. Beebe, The present and future role of microfluidics in biomedical research,
728 *Nature*. 507 (2014) 181–189. <https://doi.org/10.1038/nature13118>.
729 [2] L. Jiao, Q. Xu, J. Tong, S. Liu, Y. Hu, Q. Guo, H. Wu, W. Li, Q. Zhao, R. Chen, Facile preparation of pliable

730 superamphiphobic papers with high and durable liquid repellency for anti-corrosion and open surface microfluidics,
731 Appl. Surf. Sci. 606 (2022) 154845. <https://doi.org/https://doi.org/10.1016/j.apsusc.2022.154845>.

732 [3] H. Šířpová-Jungová, L. Jurgová, E. Hemmerová, J. Homola, Interaction of Tris with DNA molecules and
733 carboxylic groups on self-assembled monolayers of alkanethiols measured with surface plasmon resonance, Appl.
734 Surf. Sci. 546 (2021) 148984. <https://doi.org/https://doi.org/10.1016/j.apsusc.2021.148984>.

735 [4] N.S. Bhise, J. Ribas, V. Manoharan, Y.S. Zhang, A. Polini, S. Massa, M.R. Dokmeci, A. Khademhosseini,
736 Organ-on-a-chip platforms for studying drug delivery systems., J. Control. Release Off. J. Control. Release Soc.
737 190 (2014) 82–93. <https://doi.org/10.1016/j.jconrel.2014.05.004>.

738 [5] C. Dincer, R. Bruch, E. Costa-Rama, M.T. Fernandez-Abedu, A. Merkoci, A. Manz, G.A. Urban, F. Guder,
739 Disposable Sensors in Diagnostics, Food, and Environmental Monitoring, Adv. Mater. 31 (2019).
740 <https://doi.org/10.1002/adma.201806739> WE - Science Citation Index Expanded (SCI-EXPANDED).

741 [6] D.T. Chiu, A.J. deMello, D. Di Carlo, P.S. Doyle, C. Hansen, R.M. Maceiczky, R.C.R. Wootton, Small but
742 Perfectly Formed? Successes, Challenges, and Opportunities for Microfluidics in the Chemical and Biological
743 Sciences, Chem. 2 (2017) 201–223. <https://doi.org/https://doi.org/10.1016/j.chempr.2017.01.009>.

744 [7] E.B. Hua, Y. Zhang, K.Y. Yun, W.J. Pan, Y. Liu, S.X. Li, Y. Wang, R. Tu, M. Wang, Whole-Cell Biosensor
745 and Producer Co-cultivation-Based Microfluidic Platform for Screening *Saccharopolyspora erythraea* with Hyper,
746 ACS Synth. Biol. (2022). <https://doi.org/10.1021/acssynbio.2c00102>.

747 [8] O.Z.- Chebotarev, High Throughput Microfluidic Platform Capable of Mimicking Key Vascular
748 Microenvironments, University of Toronto (Canada), Ontario, Canada, 2013.

749 [9] H.W. Gao, C.L. Yan, W. Wu, J. Li, Application of Microfluidic Chip Technology in Food Safety Sensing,
750 SENSORS. 20 (2020). <https://doi.org/10.3390/s20061792>.

751 [10] C.W. Tsao, Polymer microfluidics: Simple, low-cost fabrication process bridging academic lab research to
752 commercialized production, Micromachines. 7 (2016). <https://doi.org/10.3390/mi7120225>.

753 [11] Y. Xu, Y.L. Ni, D.S. Li, Focus on the Microfluidic Chip Papers in Chinese Journal of Analytical Chemistry in
754 2010, CHINESE J. Anal. Chem. 39 (2011) 1936–1939. <https://doi.org/10.3724/SP.J.1096.2011.01936>.

755 [12] T.A. Duncombe, A.M. Tentori, A.E. Herr, Microfluidics: reframing biological enquiry, Nat. Rev. Mol. Cell
756 Biol. 16 (2015) 554–567. <https://doi.org/10.1038/nrm4041>.

757 [13] B. Liu, J. Cao, B. Hong, H. You, T. Li, Z. Yu, D. Li, B. Liang, N. Gan, A microfluidic chip platform based on
758 Pt nanozyme and magnetized phage composite probes for dual-mode detecting and imaging pathogenic bacteria
759 viability., Talanta. 275 (2024) 126067. <https://doi.org/10.1016/j.talanta.2024.126067>.

760 [14] G. Gharib, İ. Bütün, Z. Muganlı, G. Kozalak, İ. Namlı, S.S. Sarraf, V.E. Ahmadi, E. Toyran, A.J. van Wijnen,
761 A. Koşar, Biomedical Applications of Microfluidic Devices: A Review, Biosensors. 12 (2022).
762 <https://doi.org/10.3390/bios12111023>.

763 [15] P. Pattanayak, S.K. Singh, M. Gulati, S. Vishwas, B. Kapoor, D.K. Chellappan, K. Anand, G. Gupta, N.K. Jha,
764 P.K. Gupta, P. Prasher, K. Dua, H. Dureja, D. Kumar, V. Kumar, Microfluidic chips: recent advances, critical
765 strategies in design, applications and future perspectives, Microfluid. Nanofluidics. 25 (2021) 99.
766 <https://doi.org/10.1007/s10404-021-02502-2>.

767 [16] R. Riahi, A. Tamayol, S.A.M. Shaegh, A.M. Ghaemmaghami, M.R. Dokmeci, A. Khademhosseini,
768 Microfluidics for advanced drug delivery systems, Curr. Opin. Chem. Eng. 7 (2015) 101–112.

769 <https://doi.org/https://doi.org/10.1016/j.coche.2014.12.001>.

770 [17] N. Xiang, Z. Ni, *Microfluidics for Biomedical Applications*, *Biosensors*. 13 (2023).

771 <https://doi.org/10.3390/bios13020161>.

772 [18] K. Giri, C.-W. Tsao, *Recent Advances in Thermoplastic Microfluidic Bonding*, *Micromachines*. 13 (2022).

773 <https://doi.org/10.3390/mi13030486>.

774 [19] B. Zhao, Y. Qiang, W. Wu, B. Jiang, *Tuning power ultrasound for enhanced performance of thermoplastic*

775 *micro-injection molding: Principles, methods, and performances*, *Polymers (Basel)*. 13 (2021).

776 <https://doi.org/10.3390/polym13172877>.

777 [20] P.N. Immanuel, C.-C. Chiang, C.-R. Yang, M. Subramani, T.-H. Lee, S.-J. Huang, *Surface activation of*

778 *poly(methyl methacrylate) for microfluidic device bonding through a H₂O plasma treatment linked with a low-*

779 *temperature annealing*, *J. Micromechanics Microengineering*. 31 (2021) 55004. [https://doi.org/10.1088/1361-](https://doi.org/10.1088/1361-6439/abf034)

780 [6439/abf034](https://doi.org/10.1088/1361-6439/abf034).

781 [21] A. Shakeri, S. Khan, N.A. Jarad, T.F. Didar, *The Fabrication and Bonding of Thermoplastic Microfluidics: A*

782 *Review*, *Materials (Basel)*. 15 (2022). <https://doi.org/10.3390/ma15186478>.

783 [22] A. Welle, E. Gottwald, *UV-Based Patterning of Polymeric Substrates for Cell Culture Applications*, *Biomed.*

784 *Microdevices*. 4 (2002) 33–41. <https://doi.org/10.1023/A:1014267712144>.

785 [23] R. Paoli, D. Di Giuseppe, M. Badiola-Mateos, E. Martinelli, M.J. Lopez-Martinez, J. Samitier, *Rapid*

786 *Manufacturing of Multilayered Microfluidic Devices for Organ on a Chip Applications*, *Sensors*. 21 (2021).

787 <https://doi.org/10.3390/s21041382>.

788 [24] N.X.T. Le, K.T.L. Trinh, N.Y. Lee, *Poly(acrylic acid) as an adhesion promoter for UV-assisted thermoplastic*

789 *bonding: Application for the in vitro construction of human blood vessels*, *Mater. Sci. Eng. C*. 122 (2021) 111874.

790 <https://doi.org/https://doi.org/10.1016/j.msec.2021.111874>.

791 [25] H.D. Lynh, C. Pin-Chuan, *Novel solvent bonding method for creation of a three-dimensional, non-planar,*

792 *hybrid PLA/PMMA microfluidic chip*, *Sensors Actuators A Phys*. 280 (2018) 350–358.

793 <https://doi.org/https://doi.org/10.1016/j.sna.2018.08.002>.

794 [26] H. Persson, S. Park, M. Mohan, K.K. Cheung, C.A. Simmons, E.W.K. Young, *Rapid assembly of PMMA*

795 *microfluidic devices with PETE membranes for studying the endothelium*, *Sensors Actuators B Chem*. 356 (2022)

796 131342. <https://doi.org/https://doi.org/10.1016/j.snb.2021.131342>.

797 [27] B. Zhao, W. Wu, M. Zhou, B. Jiang, G. Ziegmann, *Highly dynamic tempered in-mold thermocompression*

798 *bonding of microfluidic chips: process characteristics and bonding performances*, *J. Mater. Res. Technol*. 24 (2023)

799 639–652. <https://doi.org/10.1016/j.jmrt.2023.03.040>.

800 [28] G. Kulsharova, N. Dimov, M.P.C. Marques, N. Szita, F. Baganz, *Simplified immobilisation method for*

801 *histidine-tagged enzymes in poly(methyl methacrylate) microfluidic devices*, *N. Biotechnol*. 47 (2018) 31–38.

802 <https://doi.org/https://doi.org/10.1016/j.nbt.2017.12.004>.

803 [29] R. Sivakumar, N.Y. Lee, *Microfluidic device fabrication mediated by surface chemical bonding*, *Analyst*. 145

804 (2020) 4096–4110. <https://doi.org/10.1039/d0an00614a>.

805 [30] B. Acherjee, A.S. Kuar, S. Mitra, D. Misra, S. Acharyya, *Experimental investigation on laser transmission*

806 *welding of PMMA to ABS via response surface modeling*, *Opt. Laser Technol*. 44 (2012) 1372–1383.

807 <https://doi.org/https://doi.org/10.1016/j.optlastec.2011.12.029>.

808 [31] D. Podbiel, L. Boecking, H. Bott, J. Kassel, D. Czurratis, F. Laermer, R. Zengerle, J. Hoffmann, From CAD to
809 microfluidic chip within one day: rapid prototyping of lab-on-chip cartridges using generic polymer parts, *J.*
810 *Micromechanics Microengineering*. 30 (2020) 115012. <https://doi.org/10.1088/1361-6439/aba5dd>.
811 [32] K. Kistrup, C.E. Poulsen, M.F. Hansen, A. Wolff, Ultrasonic welding for fast bonding of self-aligned structures
812 in lab-on-a-chip systems, *Lab Chip*. 15 (2015) 1998–2001. <https://doi.org/10.1039/c5lc00174a>.
813 [33] S.W. Li, J.H. Xu, Y.J. Wang, Y.C. Lu, G.S. Luo, Low-temperature bonding of poly-(methyl methacrylate)
814 microfluidic devices under an ultrasonic field, *J. Micromechanics Microengineering*. 19 (2009) 15035.
815 <https://doi.org/10.1088/0960-1317/19/1/015035>.
816 [34] K.F. Lei, S. Ahsan, N. Budraa, W.J. Li, J.D. Mai, Microwave bonding of polymer-based substrates for
817 potential encapsulated micro/nanofluidic device fabrication, *Sensors Actuators, A Phys.* 114 (2004) 340–346.
818 <https://doi.org/10.1016/j.sna.2003.12.018>.
819 [35] A.A. Yussuf, I. Sbarski, J.P. Hayes, M. Solomon, N. Tran, Microwave welding of polymeric-microfluidic
820 devices, *J. Micromechanics Microengineering*. 15 (2005) 1692–1699. <https://doi.org/10.1088/0960-1317/15/9/011>.
821 [36] A.A. Yussuf, I. Sbarski, M. Solomon, N. Tran, J.P. Hayes, Sealing of polymeric-microfluidic devices by using
822 high frequency electromagnetic field and screen printing technique, *J. Mater. Process. Technol.* 189 (2007) 401–
823 408. <https://doi.org/10.1016/j.jmatprotec.2007.02.013>.
824 [37] S.R. Mahmoodi, P.-K. Sun, M. Mayer, R.S. Besser, Gas-assisted thermal bonding of thermoplastics for the
825 fabrication of microfluidic devices, *Microsyst. Technol.* 25 (2019) 3923–3932. [https://doi.org/10.1007/s00542-019-](https://doi.org/10.1007/s00542-019-04380-9)
826 [04380-9](https://doi.org/10.1007/s00542-019-04380-9).
827 [38] P.M. Kristiansen, A. Karpik, J. Werder, M. Guilherme, M. Grob, Thermoplastic Microfluidics, *Methods Mol.*
828 *Biol.* 2373 (2022) 39–55. https://doi.org/10.1007/978-1-0716-1693-2_3.
829 [39] A. Shakeri, N. Abu Jarad, S. Khan, T.F. Didar, Bio-functionalization of microfluidic platforms made of
830 thermoplastic materials: A review, *Anal. Chim. Acta.* 1209 (2022). <https://doi.org/10.1016/j.aca.2021.339283>.
831 [40] K.T.L. Trinh, D.A. Thai, N.Y. Lee, Bonding Strategies for Thermoplastics Applicable for Bioanalysis and
832 Diagnostics, *MICROMACHINES*. 13 (2022). <https://doi.org/10.3390/mi13091503>.
833 [41] C.W. Tsao, Polymer microfluidics: Simple, low-cost fabrication process bridging academic lab research to
834 commercialized production, *Micromachines*. 7 (2016). <https://doi.org/10.3390/mi7120225>.
835 [42] M. Matteucci, A. Heiskanen, K. Zór, J. Ennéus, R. Taboryski, Comparison of Ultrasonic Welding and
836 Thermal Bonding for the Integration of Thin Film Metal Electrodes in Injection Molded Polymeric Lab-on-Chip
837 Systems for Electrochemistry, *Sensors*. 16 (2016). <https://doi.org/10.3390/s16111795>.
838 [43] B. Zhao, F. Mo, W. Wu, B. Jiang, G. Ziegmann, Deformation patterns and coordination mechanisms of cross-
839 size microchannels during thermocompression bonding process, *J. Mater. Res. Technol.* 26 (2023) 3701–3709.
840 <https://doi.org/10.1016/j.jmrt.2023.08.141>.
841 [44] C. Wei, H. Gu, Y.C. Gu, Y.H. Huang, D.X. Cheng, Z.Q. Li, L. Li, Abnormal interfacial bonding mechanisms
842 of multi-material additive-manufactured tungsten-stainless steel sandwich structure, *Int. J. Extrem. Manuf.* 4 (2022).
843 <https://doi.org/10.1088/2631-7990/ac5f10>.
844 [45] C. Wei, Z.Z. Zhang, D.X. Cheng, Z. Sun, M.H. Zhu, L. Li, An overview of laser-based multiple metallic
845 material additive manufacturing: from macro- to micro-scales, *Int. J. Extrem. Manuf.* 3 (2021).
846 <https://doi.org/10.1088/2631-7990/abce04>.

- 847 [46] A. Zolfaghari, T.T. Chen, A.Y. Yi, Additive manufacturing of precision optics at micro and nanoscale, *Int. J.*
848 *Extrem. Manuf.* 1 (2019). <https://doi.org/10.1088/2631-7990/ab0fa5>.
- 849 [47] Z.Q. Fan, Q.Y. Tan, C.W. Kang, H. Huang, Advances and challenges in direct additive manufacturing of dense
850 ceramic oxides, *Int. J. Extrem. Manuf.* 6 (2024). <https://doi.org/10.1088/2631-7990/ad5424>.
- 851 [48] C.J. Shuai, D.S. Li, X. Yao, X. Li, C.D. Gao, Additive manufacturing of promising heterostructure for
852 biomedical applications, *Int. J. Extrem. Manuf.* 5 (2023). <https://doi.org/10.1088/2631-7990/acded2>.
- 853 [49] X.R. Li, B.Y. Zhang, T. Jakobi, Z.L. Yu, L.Q. Ren, Z.H. Zhang, Laser-based bionic manufacturing, *Int. J.*
854 *Extrem. Manuf.* 6 (2024). <https://doi.org/10.1088/2631-7990/ad3f59>.
- 855 [50] J.S. Wang, F.Z. Fang, H.J. An, S. Wu, H.M. Qi, Y.X. Cai, G.Y. Guo, Laser machining fundamentals: micro,
856 nano, atomic and close-to-atomic scales, *Int. J. Extrem. Manuf.* 5 (2023). <https://doi.org/10.1088/2631-7990/acb134>.
- 857 [51] X.L. Wang, D.T.T. Phan, D. Zhao, S.C. George, C.C.W. Hughes, A.P. Lee, An on-chip microfluidic pressure
858 regulator that facilitates reproducible loading of cells and hydrogels into microphysiological system platforms, *Lab*
859 *Chip.* 16 (2016) 868–876. <https://doi.org/10.1039/c5lc01563d>.
- 860 [52] S.Q. Hu, X. Huan, Y. Liu, S.X. Cao, Z.R. Wang, J.T. Kim, Recent advances in meniscus-on-demand three-
861 dimensional micro- and nano-printing for electronics and photonics, *Int. J. Extrem. Manuf.* 5 (2023).
862 <https://doi.org/10.1088/2631-7990/acdf2d>.
- 863 [53] J.M. Castro, S. Rajaraman, Experimental and Modeling Based Investigations of Process Parameters on a
864 Novel, 3D Printed and Self-Insulated 24-Well, High-Throughput 3D Microelectrode Array Device for Biological
865 Applications, *J. MICROELECTROMECHANICAL Syst.* 31 (2022) 358–371.
866 <https://doi.org/10.1109/JMEMS.2022.3160663>.
- 867 [54] A. Kundu, A. Rozman, S. Rajaraman, Development of a 3D Printed, Self-Insulated, High-Throughput 3D
868 Microelectrode Array (HT-3DMEA), *J. MICROELECTROMECHANICAL Syst.* 29 (2020) 1091–1093.
869 <https://doi.org/10.1109/JMEMS.2020.3003644>.
- 870 [55] A. Kundu, L. McCoy, N. Azim, H. Nguyen, C.M. Didier, T. Ausaf, A.D. Sharma, J.L. Curley, M.J. Moore, S.
871 Rajaraman, Fabrication and Characterization of 3D Printed, 3D Microelectrode Arrays for Interfacing with a
872 Peripheral Nerve-on-a-Chip, *ACS Biomater. Sci. Eng.* 7 (2021) 3018–3029.
873 <https://doi.org/10.1021/acsbomaterials.0c01184>.
- 874 [56] T.N.A. Vo, P.-C. Chen, Maximizing interfacial bonding strength between PDMS and PMMA substrates for
875 manufacturing hybrid microfluidic devices withstanding extremely high flow rate and high operation pressure,
876 *Sensors Actuators A Phys.* 334 (2022) 113330. <https://doi.org/https://doi.org/10.1016/j.sna.2021.113330>.
- 877 [57] M. Madadi, A. Madadi, R. Zareifar, A. Nikfarjam, A simple solvent-assisted method for thermal bonding of
878 large-surface, multilayer PMMA microfluidic devices, *Sensors Actuators A Phys.* 349 (2023) 114077.
879 <https://doi.org/https://doi.org/10.1016/j.sna.2022.114077>.
- 880 [58] T. Guan, S. Yuket, H. Cong, D.W. Carton, N. Zhang, Permanent Hydrophobic Surface Treatment Combined
881 with Solvent Vapor-Assisted Thermal Bonding for Mass Production of Cyclic Olefin Copolymer Microfluidic
882 Chips, *ACS Omega.* 7 (2022) 20104–20117. <https://doi.org/10.1021/acsomega.2c01948>.
- 883 [59] M. Busek, S. Nøvik, A. Aizenshtadt, M. Amirolo-Martinez, T. Combriat, S. Grünzner, S. Krauss,
884 Thermoplastic Elastomer (TPE)–Poly(Methyl Methacrylate) (PMMA) Hybrid Devices for Active Pumping PDMS-
885 Free Organ-on-a-Chip Systems, *Biosensors.* 11 (2021). <https://doi.org/10.3390/bios11050162>.

886 [60] J. Cheon, S. Kim, Intermediate layer-based bonding techniques for polydimethylsiloxane/digital light
887 processing 3D-printed microfluidic devices, *J. Micromechanics Microengineering*. 29 (2019) 95005.
888 <https://doi.org/10.1088/1361-6439/ab27d3>.

889 [61] X. Ku, G. Zhuang, G. Li, A universal approach for irreversible bonding of rigid substrate-based microfluidic
890 devices at room temperature, *Microfluid. Nanofluidics*. 22 (2018) 17. <https://doi.org/10.1007/s10404-018-2039-3>.

891 [62] N. Ling, J.S. Lee, N.Y. Lee, Solvent-assisted low-temperature and low-pressure poly(methylmethacrylate)
892 bonding coupled with selective microchannel hydrophobic coating for reliable sealing, *Sensors Actuators A Phys.*
893 265 (2017) 168–173. <https://doi.org/https://doi.org/10.1016/j.sna.2017.08.023>.

894 [63] A. Bamshad, A. Nikfarjam, H. Khaleghi, A new simple and fast thermally-solvent assisted method to bond
895 PMMA–PMMA in micro-fluidics devices, *J. Micromechanics Microengineering*. 26 (2016) 65017.
896 <https://doi.org/10.1088/0960-1317/26/6/065017>.

897 [64] S. Hassanpour-Tamrin, A. Sanati-Nezhad, A. Sen, A simple and low-cost approach for irreversible bonding of
898 polymethylmethacrylate and polydimethylsiloxane at room temperature for high-pressure hybrid microfluidics, *Sci.*
899 *Rep.* 11 (2021) 4821. <https://doi.org/10.1038/s41598-021-83011-8>.

900 [65] B. Zhao, W. Wu, B. Jiang, The in-mold thermocompression bonding process of microfluidic chips based on the
901 highly dynamic variotherm technology: Process characteristics, in: *NanoMan 2022 AETS 2022 - 2022 8th Int. Conf.*
902 *Nanomanufacturing 4th AET Symp. ACSM Digit. Manuf., 2022*: pp. 1–6. [https://doi.org/10.1109/Nanoman-](https://doi.org/10.1109/Nanoman-AETS56035.2022.10119480)
903 [AETS56035.2022.10119480](https://doi.org/10.1109/Nanoman-AETS56035.2022.10119480).

904