Photoresponsive Polymer-Based Biomimetic Contractile Units as Building Block for Artificial Muscles

Macromolecular Materials and Engineering
www.mame-journal.de

Photoresponsive Polymer-Based Biomimetic Contractile Units as Building Block for Artificial Muscles

Giulia Vitale, Bruno Grandinetti, Silvia Querceto, Daniele Martella, Chiara Tesi, Corrado Poggesi, Elisabetta Cerbai, Diederik S. Wiersma, Camilla Parmeggiani, Cecilia Ferrantini,* and Leonardo Sacconi*

Loss of muscular mechanical function occurs in several diseases affecting millions of people worldwide, including heart failure, stroke, and neuromuscular disorders. To date, no medical or surgical treatments can restore muscular contractility, and the development of artificial muscles is of extreme interest. Mimicking biological muscles, which are optimized systems displaying quick reaction times, is not trivial; only few examples are reported, mainly focused on the use of biomimetic smart materials. Among them, liquid crystalline elastomers (LCEs) can be biocompatible, show contraction parameters comparable to those of native striated muscles, and are able to effectively potentiate cardiac contraction in vitro. To go further and develop in vivo implantable devices, the integration of the stimulation system with the LCE material represents an essential step. Here, a light-stimulated biomimetic contractile unit (BCU), combining ultra-thin photoresponsive LCE films and mini-LED (mLED) matrixes is described. BCU performance (in terms of extent and kinetics of contractile force and shortening) can be fine-tuned by modulating both mLED light power and spatial stimulation patterns, allowing to reproduce mechanical dynamics of native muscles. These results pave the way for the development of novel LCE-based contraction assist devices for cardiac, skeletal, or smooth muscle support by assembling multiple BCUs.

1. Introduction

Current medical or surgical treatments cannot restore muscular contractility and, so far, materials or devices have failed to reproduce natural muscle function.[1,2] Biological muscles are optimized systems that are relatively similar in all species and exhibit quick reaction times in the order of milliseconds. Natural muscles can provide billions of work cycles involving tension development or movement and can increase/change their strength and stiffness in response to several mechanical needs. These features are difficult to be fully mimicked by artificial devices. However, the function of native muscles can be reproduced, at least in part, by smart materials, which are able to respond to external stimuli.[3,4] Among them, liquid crystalline elastomers (LCEs) can deform in a reversible manner, generating movement or tension during actuation.[5] This unique behavior is determined by the combination of the features of liquid crystals (LCs) with

G. Vitale, S. Querceto, C. Tesi, C. Poggesi, C. Ferrantini
Department of Experimental and Clinical Medicine
University of Florence
Largo Brambilla 3, Firenze 50134, Italy
E-mail: cecilia.ferrantini@unifi.it

B. Grandinetti, D. Martella, C. Poggesi, E. Cerbai, D. S. Wiersma, C. Parmeggiani, C. Ferrantini, L. Sacconi
European Laboratory for Non Linear Spectroscopy (LENS)
via Nello Carrara 1, Sesto Fiorentino 50019, Italy
E-mail: camilla.parmeggiani@lens.unifi.it

The ORCID identification number(s) for the author(s) of this article can be found under https://doi.org/10.1002/mame.202200187

DOI: 10.1002/mame.202200187

D. Martella, D. S. Wiersma, C. Parmeggiani
Istituto Nazionale di Ricerca Metrologica (INRiM)
Strada delle Cacce 91, Torino 10135, Italy

E. Cerbai
Department of Neurosciences
Psychology
Drug Research and Child Health (NEUROFARBA)
University of Florence
Viale Pieraccini 6, Firenze 50139, Italy

D. S. Wiersma, L. Sacconi
Istituto Nazionale di Ottica, Consiglio Nazionale delle Ricerche
via Nello Carrara,1, Sesto Fiorentino 50019, Italy

D. S. Wiersma
Department of Physics and Astronomy
University of Florence
via Sansone 1, Sesto Fiorentino 50019, Italy

C. Parmeggiani
Department of Chemistry
University of Florence
via della Lastruccia 3-13, Sesto Fiorentino 50019, Italy

the properties of elastomers. Indeed, LCEs possess the orientational order at molecular level and sensitivity to different external stimuli (temperature, light and others) of LCs, combined with the elasticity and endurance to mechanical stresses that are typical of elastomers.[6–10]

Adjusting their composition, e.g., by modulating the crosslinking degree[11] or changing the mesogenic units,[12,13] actuation kinetics and mechanical properties can be finely modulated.[7] For instance, previous findings on the possibility to exploit LCEs in tissue engineering reported the use of these materials to mimic intervertebral disks[14] or muscles.[15]

Regarding the latter, we have recently demonstrated how a selected custom-made palette of LCEs can behave like artificial cardiac muscles in terms of active and passive mechanical properties generating, upon light stimulation, maximal tensions comparable to those measured from maximally calcium-activated striated muscles (in the order of 400 mN mm^{-2}).[16,17]

Notably, we reported that LCE strips mounted onto a murine left-ventricle trabecula could effectively enhance muscle contraction, thus providing new insights on the design of novel contraction assist devices. However, the development of an implantable biomimetic contractile unit (BCU) requires a full integration of the active LCE material with the light stimulus.

On this side, many studies related to light-driven LCEs focused on a variety of light sources (i.e., lasers, lamps, optical fibers) that allow a remote control over the actuators,[18–24] but still presenting many limitations for biomedical purposes.[16] Among them, light penetration through turbid or opaque media (such as biological tissues) is very low, thus preventing the deformation of photo-stimulated materials in such environments. Possible solutions can be the integration of LCE structure on the top of an optical fiber[25] or using LCEs as optical fibers.[26] In both cases, only tethered structures with limited size and shape can be obtained and they do not represent a solution to develop BCUs on large scales. For this reason, a different strategy for the integration of the light source with the contractile materials results mandatory toward the development of stimulable biomedical devices. In this work, we present and characterize the first prototype of a BCU made by interposing a thin LCE film between two matrixes of mini-LEDs (mLEDs). This study not only describes the first modulable artificial muscle, but also provides new insights on an integrated LCE-mLED system, for the development of more complex contraction assist devices.

2. Results and Discussion

2.1. Active Material Optimization and BCU Design

The working principle of the BCU mimics human skeletal and cardiac muscle, where sarcomeres are the smallest autonomous contractile units in myocytes. Their reversible shortening is mediated by thin actin filaments sliding upon thick myosin filaments, following an increase of intracellular calcium concentration (**Figure 1**a). Sarcomeres are assembled in series in subcellular structures named myofibrils. The contemporary shortening of the rows of sarcomeres in the myofibrils leads to the macroscopic shortening of the striated muscle.

To mimic the working principle of natural contractile units, the BCU was built using an LCE-based active material able to reversibly contract, when stimulated by light, along a specific direction that corresponds to the LC alignment direction (Figure 1b, Movie S1, Supporting Information). The photoresponsive material undergoes a microscopic change in the network alignment when azobenzene response is triggered upon illumination and the addition of microscopic molecular motions in series is translated into a macroscopic shape change.

In particular, a polymeric film was prepared via photopolymerization of an acrylate-based mixture of reactive LC compounds in the nematic phase (Figure 1c).[11,16] The mixture was composed of a monoacrylate monomer (C6BP) and a diacrylate crosslinker (RM257), both presenting a nematic mesophase, and was doped with Disperse Red 1 Acrylate (DR1 Acrylate), to induce a photo responsiveness. To trigger the radical polymerization reaction, a UV-responsive photoinitiator (Irgacure 369) was used (Figure 1c). Due to the absorption properties of this dye, we selected blue-mLEDs as light source for the activation of the contractile units, since their emission spectrum fits the maximum of absorption of the material (Figure 1d). The LCE material displays homogeneous planar alignment, with molecules parallel to the film surface and well-aligned along the nematic director. This alignment determines the contraction direction, along the molecular director, during the activation of the material (Figure 1b).

The preparation of the LCE films followed the LC cell technique, commonly used to align low-molecular-weight LCs.[9,11,27] Glass slides composing the cell are coated with poly(vinyl alcohol) (PVA) as a sacrificial layer, which is uniaxially rubbed. This way LC molecules reoriented following the direction imposed by rubbing through weak interactions. The LC mixture is infiltrated in its isotropic phase in the cell via capillary action. Then, the system is cooled down to the nematic phase, obtaining a well aligned LC sample, and polymerized and crosslinked by UV, freezing such alignment in the network (**Figure 2**).

The prototype of the modulable BCU was made by interposing an ultra-thin LCE strip between two matrixes of blue mLEDs, prepared by assembling eight blue mLEDs on a printed circuit board (PCB) with a pixel pitch of 0.75 mm (**Figure 3**a, b). The LCE films were cut into strips, following LC alignment direction, whose dimensions, i.e., 8 mm length × 0.75 mm width, were selected according to mLED matrix size and illumination pattern. The thickness of the LCEs was chosen based on the absorption properties of the material with respect to the blue light stimulus. Specifically, by using a 10 μm thick LCE film illuminated from both sides, we guarantee a uniform illumination through the whole LCE depth with an estimated intensity gap between the surface and the central portion in the order of 28% (Figure 3c). Finally, the distance between the mLED matrix and the LCE (200 μm) was chosen according to the mLED divergence cone to guarantee a proper overlap between two adjacent illumination spots (Figure 3d).

2.2. BCU Mechanical Characterization

To characterize its photomechanical properties, the BCU was vertically mounted, between a force transducer on top and a hanging load below, as shown in **Figure 4**a. A first characterization was carried out under isometric condition, by hanging loads that exceeded the expected maximum load that the BCU

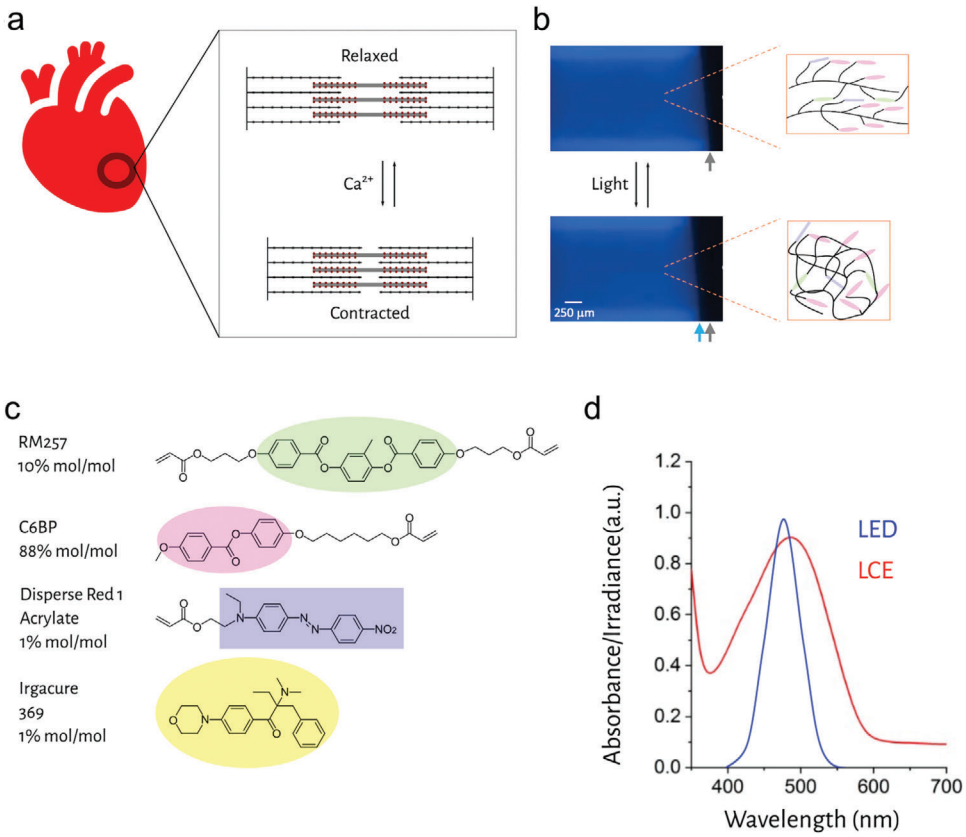

Figure 1. Working mechanism of the biomimetic contractile unit. a) Scheme of contraction in human cardiac sarcomeres, the contractile units of all striated muscles. b) Contraction of the LCE under illumination. Gray and blue arrows indicated the edge of the LCE strip before and after illumination respectively. Conformations of LCE molecules with and without light are shown in the right inset. c) Composition of the monomer mixture used to fabricate the BCU. d) Emission spectrum of the mLEDs (blue line) and the absorption spectrum of tested LCE (red line).

could lift. Monitoring the force generation obtained by the BCU, following a cumulative activation of two independent mLEDs facing each other, the force amplitude increased, as expected, with the number of activated mLEDs (Figure 4b). Interestingly, the cumulative effect shown during the activation of mLEDs facing each other led to a force amplitude that was more than twice that obtained with a single side illumination (2.3 ± 0.3), probably due to a non-linear relationship between the force development and the light power applied to the material.

In this respect, the dependence of the force generation process on light power was monitored by using a single illumination unit (ILU; two mLEDs facing each other) and increasing the light power from 0 to 22 mW (Figure 4c and Figure S1, Supporting Information). As expected from our previous investigations, a non-linear behavior between the developed force and light power was observed within this range of irradiation intensity.[16] Moreover, we found that BCU activation and relaxation kinetics were positively affected by the increase in light power (Figure 4d), showing a half time in the range of few hundreds of milliseconds at the maximum illumination power. Additionally, by switching ON an increasingly number of ILUs, the force generated by the BCU was increased and the contraction kinetics became faster (Figure 4e). Interestingly, the improvement in the kinetics of activation and relaxation did not follow the same trend in the two processes (Figure S2, Supporting Information), as expected, due to the asymmetric response of the material.[28] A decrease in contraction time as a function of an increased number of activated ILUs was observed that could be attributed to a thermal effect of the light source on the LCE strip. Conversely, the increase in temperature resulted in a longer relaxation time of the system, due to the concomitant heat dissipation upon switching OFF the ILUs.

Finally, the illumination pattern could also modulate the mechanical performance of the BCU. This was demonstrated by letting each ILU operate at a constant light power of 17.8 mW and setting as reference the force generated by the BCU when a single ILU was activated. While keeping the reference ILU switched ON, one additional ILU placed at different distance was recruited demonstrating that the smaller the distance between two ILUs, the higher the force amplitude generated (**Figure 5**a,b). Importantly, the maximal force amplitude was achieved only when the two active ILUs were adjacent. Another experiment on the influence of the stimulation pattern on force amplitude was performed by simultaneously activating four ILUs differently distributed along the contractile unit (Figure 5c,d). The BCU produced a slightly higher force amplitude when two active ILUs were close to each other, while the generated tension decreased when the active ILUs were separated by inactive segments. This behavior could be explained by considering the non-linear response of the material. In fact, adjacent ILUs irradiation cones can overlap (see Figure 3d) producing higher force with respect

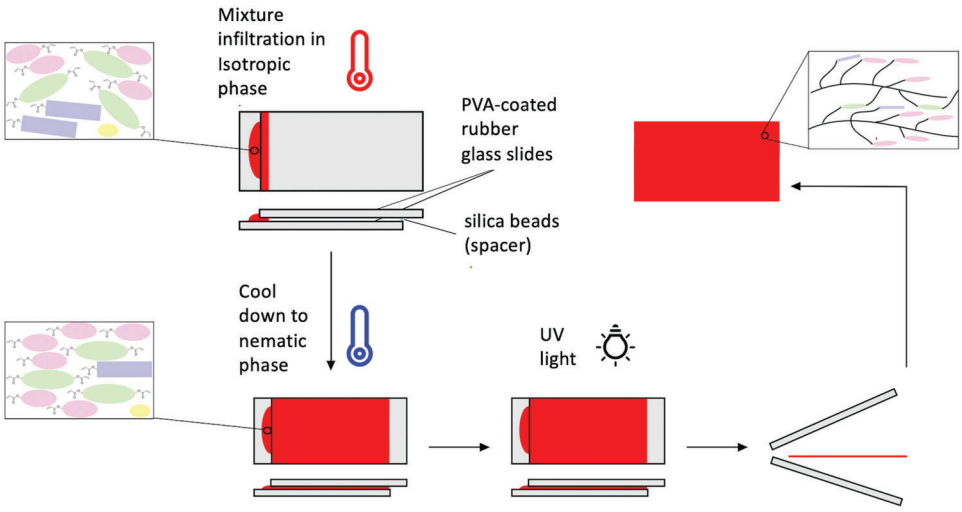

Figure 2. Scheme of the preparation of LCE films via LC cell, followed by photopolymerization and crosslinking.

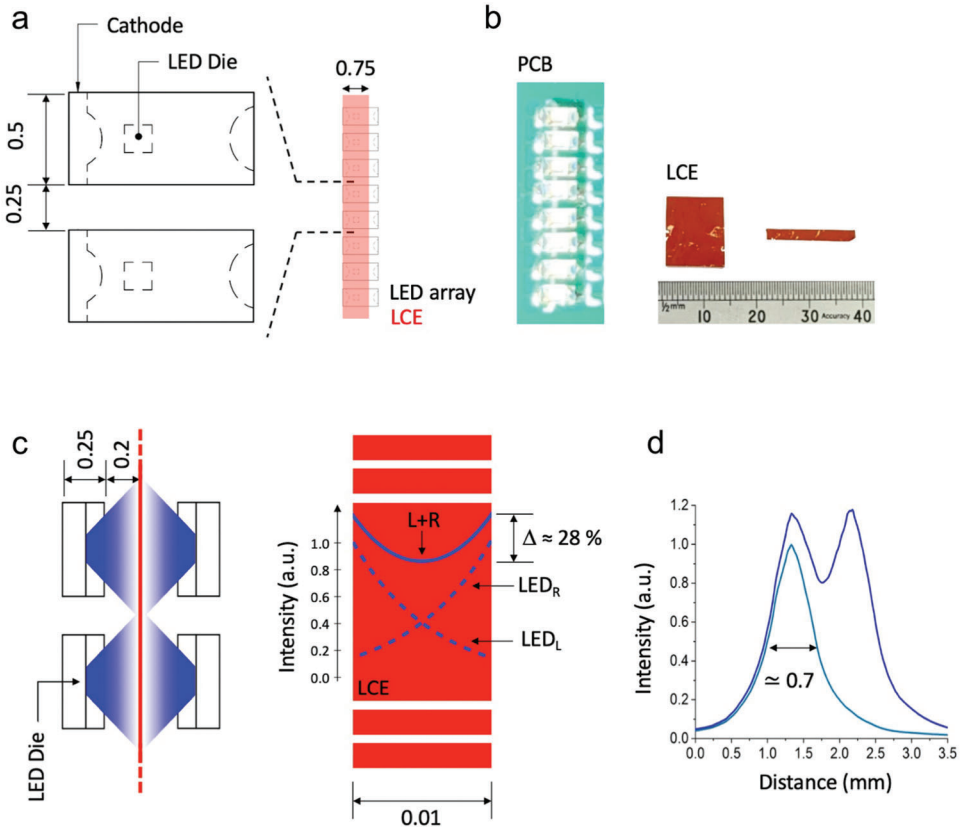

Figure 3. Design of the biomimetic contractile unit. a) Frontal view of the BCU designed prototype, composed of an ultra-thin LCE strip interposed between two arrays of eight blue mini-LEDs. b) Left: Photo of the printed circuit board (PCB) of the mini-LEDs array. Shown in scale with the scheme described on panel (a). Right: Photo of an LCE film and strip. c) Right: sagittal view of a portion of the BCU, showing two independent mLEDs facing each other with the LCE strip within. Left: estimation of light propagation inside a 10 µm thick LCE during one-side and dual-side illumination configurations. d) Illumination profile on LCE surface produced by a single mLED and two adjacent mLEDs.

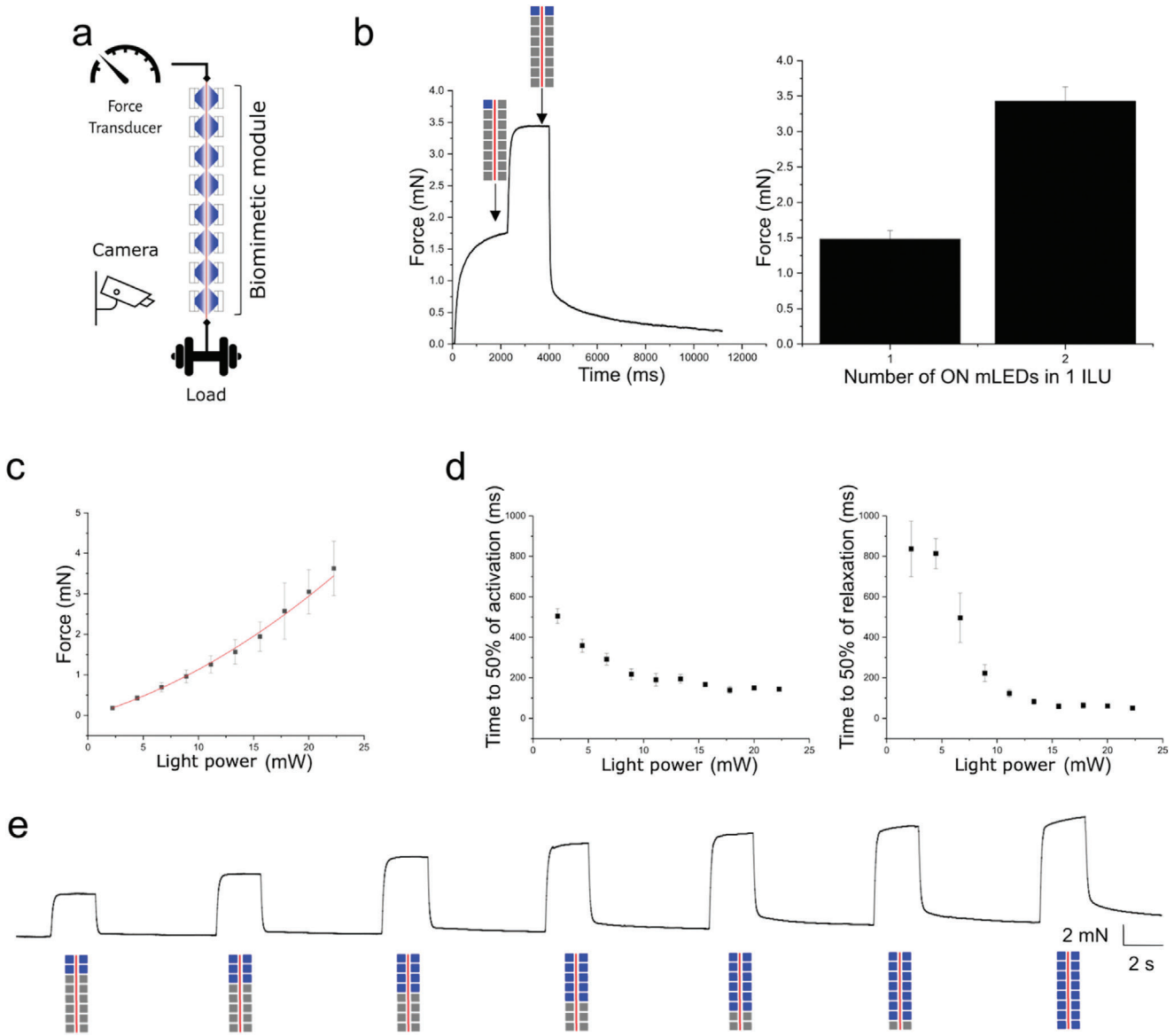

Figure 4. Mechanical characterization of the BCU. a) Experimental setup. The BCU is vertically mounted in isometric conditions. b) Force development and maximum force amplitude during the activation of one and two independent mLEDs facing each other. c) Dependence of force amplitude on single ILU light power. The red line shows the deviation from a linear fit. d) Dependence of kinetics of activation and relaxation on increasing ILU light power. e) Force generated by raising the number of activated ILUs.

to the same power distributed across the whole LCE strip. This experiment supported the design of the BCU, guaranteeing the most efficient and homogeneous illumination of the LCE strip. Overall, considering the above-mentioned results, the importance of a homogeneous illumination of the BCU to obtain higher force levels and faster contraction kinetics is highlighted.

In the view of previous findings obtained from the mechanical characterization of BCU under isometric conditions, the next step was to assess the mechanical properties of the contractile unit under isotonic conditions, thus allowing the material to shorten while lifting a specific load. To perform these experiments, two different loads were applied to the device with all ILUs operating at maximum light power (17.8 mW). Then, the BCU was characterized in terms of active force (F), displacement (ΔL), and shortening velocity (v).

Monitoring LCE strip displacement with a CMOS camera, it was shown that, like in natural muscles, the higher the load the lower the extent of shortening and shortening velocity (**Figure 6**). The LCE strip shortening was monitored by video-edge detection at the strip end where the load was attached. The shortening velocity values of the LCE strip (v_A and v_B in Figure 6b) were estimated from the maximal slope of the shortening trace. The contractile unit was activated with a t_{ON} = 1 s by recruiting all ILUs on both matrixes. In Figure 6a experiments performed under isotonic conditions with two different loads ($Load_A$ = 5 mN and $Load_B$ = 1 mN) are reported. Figure 6b shows the relation

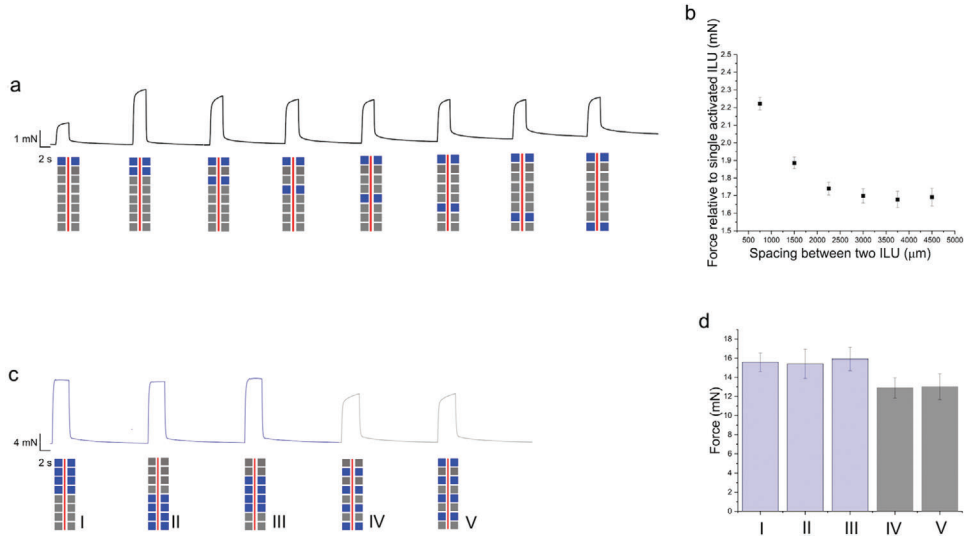

Figure 5. Effect of different illumination patterns on the force amplitude of the BCU. a) Force generated by the BCU when a single reference ILU was activated and then a second ILU placed at progressively increasing distance was simultaneously switched ON. b) Relative force generated by the BCU when the spacing between two active ILUs was varied. c) Force generated by the simultaneous activation of four ILUs differently distributed along the BCU. d) Force amplitude obtained with the different illumination patterns shown in panel (c).

between the extent of shortening after 1 s of illumination and the applied load. Specifically, it was observed that by imposing a low load (e.g., $Load_B$ = 1 mN) to the BCU, the shortening velocity of the artificial muscle approached values in the order of 0.20 muscle lengths/s, which are consistent with the shortening velocity reported for human ventricular muscle working under a low load.[29] These values are also consistent with the maximum shortening velocity reported for the cardiac β-myosin expressed in human slow skeletal fibers.[30]

Even though the displacement and generated force values proved to be lower than in shape-changing systems, previously described in the literature, the major advantage of the BCU presented in this work is the fast and miniaturized stimulation apparatus that did not rely on convective heat fluxes, resistive Joule heating and fluid-driven heating/cooling. Previously described actuation stimuli shorten the bandwidth (i.e., the range of frequencies the actuator can bear) of the devices and the kinetics of actuation, limiting their motion to longer time scales (second-to-minute intervals) compared to our device.[4,31–33] In addition, our BCU was prepared following a one-pot synthetic route based on the photopolymerization of acrylate-ended mesogens, which is versatile, rapid and easy to be performed. Other kinds of higher-load-bearing LCE systems rely on different synthetic strategies that involve, for instance, two-step crosslinking reactions with LC alignment carried out via mechanical loading or stretching.[34–37]

Finally, with the perspective of developing BCU-based contraction assist devices, the longevity of the unit was tested during continuous pulsed stimulation. Specifically, an isometrically mounted BCU was activated at 0.5 Hz stimulation frequency (i.e., t_{ON} and t_{OFF} of 500 and 1500 ms, respectively) to mimic cardiac beats, by illuminating the whole surface of the BCU.

Twitch parameters were analyzed over a period of 5 days. At day 0, the BCU produced a baseline active tension of ≈10 mN that was kept constant for the whole 5-day experiment period (Figure S3, Supporting Information), without showing any tension run-down due to dye photobleaching, as already observed in a previous work.[16]

The slow activation kinetics, compared to native muscle, are a limiting factor to obtain rapid and large force generation with LCE-based materials. **Figure 7**a shows the BCU behavior in response to progressively increased illumination times (i.e., t_{ON} from 0.25 to 5 s) and demonstrates that the maximum force value (≈16 mN) can be reached only with long illumination periods (longer than 2 s), thus precluding high force generation at fast pacing rates. As expected, peak force decreased when t_{ON} was set to a value lower than 1 s, and the BCU could generate a peak force of 4 mN using an illumination time in the order of 250 ms, i.e., the contraction time found in human ventricular myocardium.[38] On this respect, by increasing light power (obtained by varying the number of active ILUs) and reducing the t_{ON}, the BCU could replicate the rate-adaptation of twitch amplitude and duration observed in human ventricular myocardium (Figure 7b,c) mimicking the native cardiac muscle function.[38]

Notably, the excitation frequency and force amplitude of the BCU are tunable.[16] This demonstrates the possibility to modulate BCU activation parameters, in the view of its use as a cardiac contraction assist device toward a personalized medical therapy.

In terms of force production per cross-sectional area, the present prototype has mainly a proof-of-concept value and many aspects are yet to be improved to reach mechanical performance comparable to that of native muscle. The myocardium, for instance, works at sub-maximal activation, meaning that the chemical stimulus that triggers contraction (i.e., the rise of intracellular calcium concentration) is not sufficient to exploit the maximum tension level that the contractile apparatus could produce (≈200 mN mm^{-2}); the actual peak tension generated by ventricular cardiomyocytes in vivo is estimated to be in the order of 40–60 mN mm^{-2}.[38] By analogy, the BCU has a large potential mechanical output, and the trigger light stimulus can efficiently

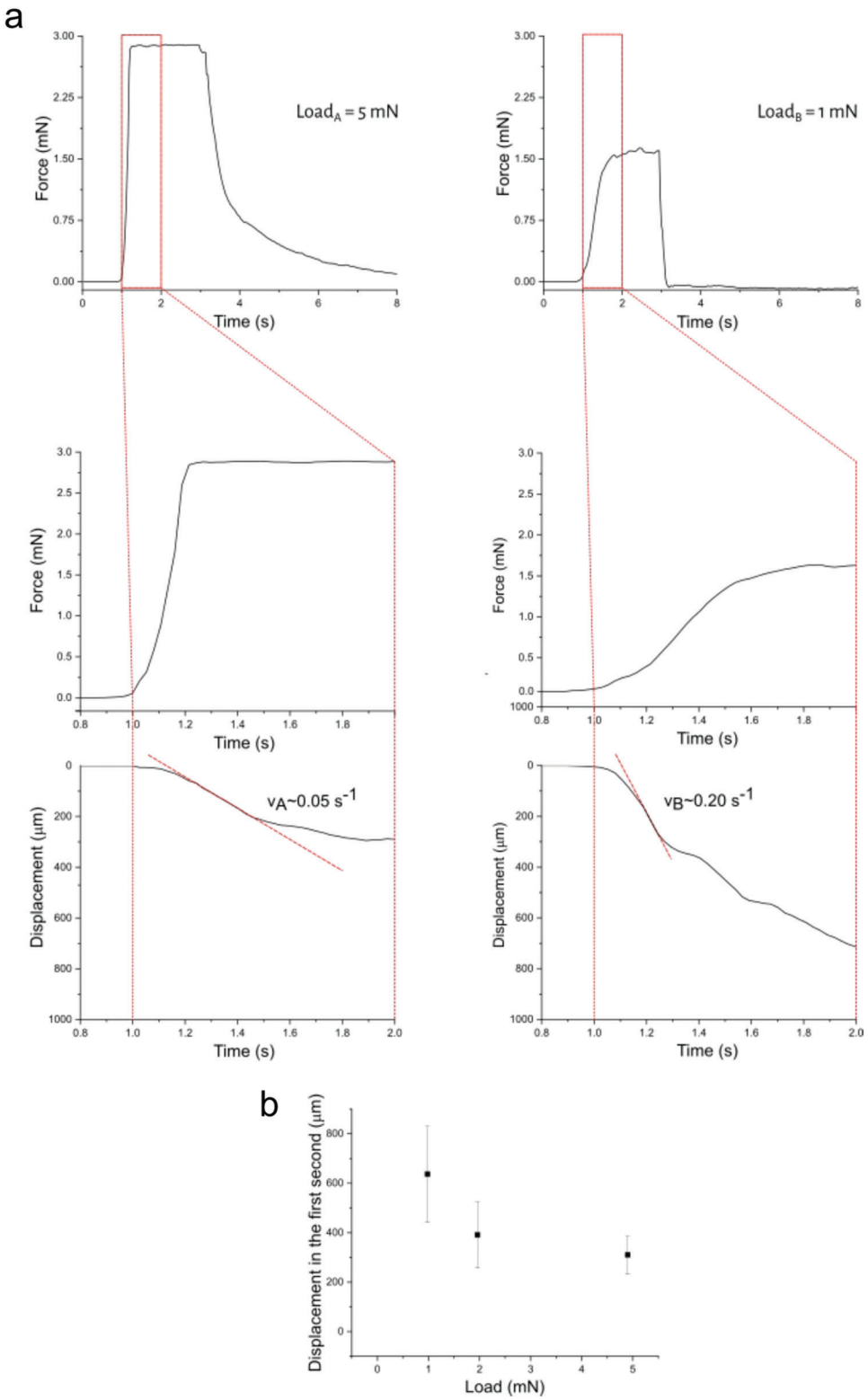

Figure 6. Mechanical properties of BCU under isotonic conditions. a) Force recorded with different afterloads ($Load_A = 5$ mN and $Load_B = 1$ mN); light is switched ON at 1 s and switched OFF at 2 s. In the red inset, force and the corresponding displacement are shown up to 1 s of light activation. The shortening velocity values of the artificial muscle are in the order of ≈0.05 s^{-1}, under $Load_A$, and ≈0.2 s^{-1}, under $Load_B$. b) Relationship between applied load and displacement at 1 s of activation.

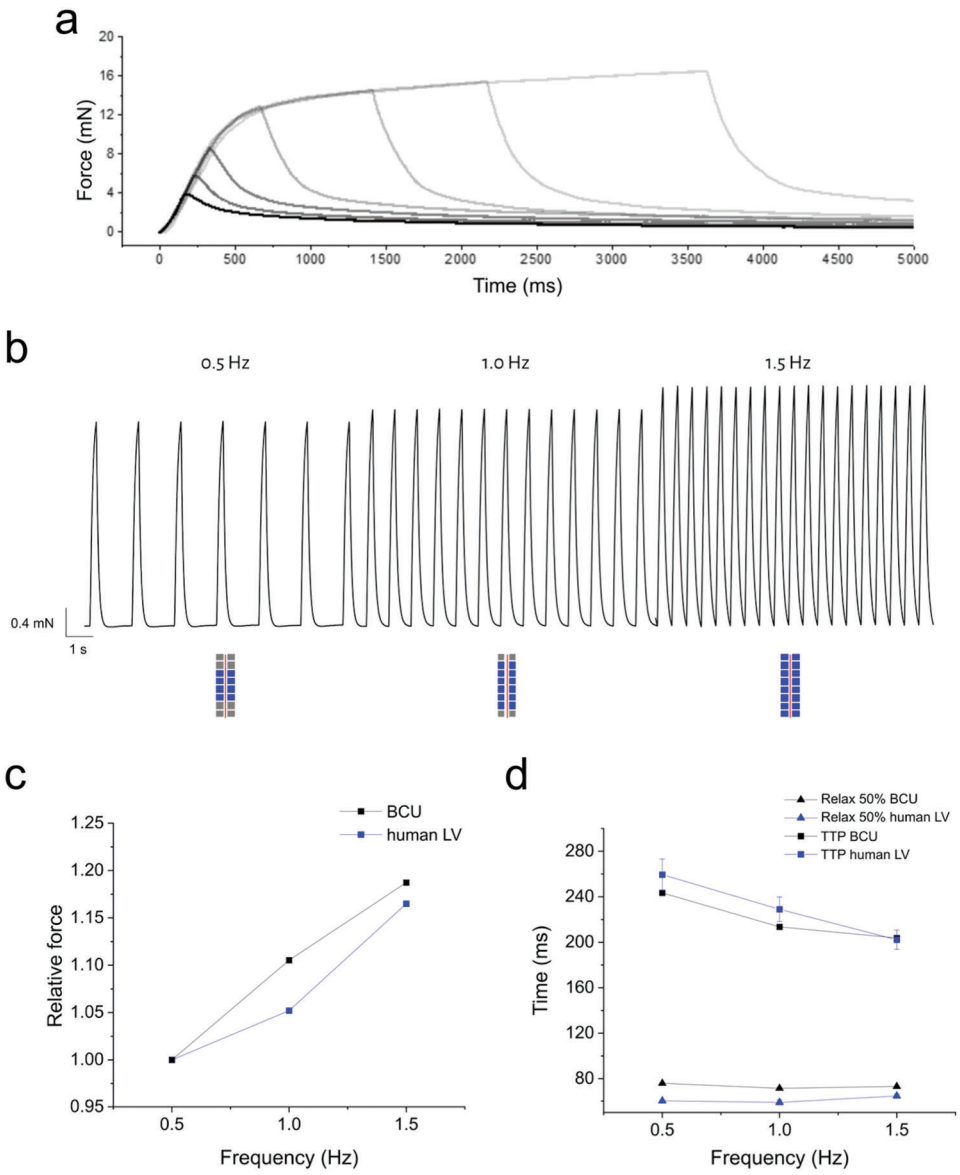

Figure 7. Force-frequency relationship of the BCU. a) Force generated by BCU activated by progressively increasing the illumination time t_{ON} (from 0.25 s to ≈4 s). b) Twitch contractions of BCU obtained by changing the number of activated mLEDs. c) Dependence of force amplitude and d) contraction kinetics on stimulation frequencies. In both panels data from BCU are compared to data from intact human left ventricular (LV) preparations.[38]

modulate the BCU contractile force. Specifically, we found (Figure 7a) that our BCU prototype can develop one quarter of maximal tension (≈4 mN) with an illumination time comparable to that of human ventricular contraction (200–250 ms).

Normalizing the maximal force that BCU can generate under isometric condition for the BCU cross-sectional area (in the order of 0.75 mm^2, see Figure 1a), a tension level of about ≈5 mN mm^{-2} can be found, which is one order of magnitude lower than that of the native muscle. Considering that, with this material, the thickness of the active layer cannot be increased due to the optical properties of the materials, in which the presence of the dye makes them opaque thus hindering light transmission through the whole thickness of the sample, a downscale in the thickness of the illumination layer is needed. As an example, by employing an illumination layer 40–50 µm thick (achievable with a micro-LED matrix) the BCU would be able to reach a tension level of about 50 mN mm^{-2}, like that developed by the working myocardium.

3. Conclusions

Despite major advances in the field of striated muscle regeneration and assistance, new devices are still needed for effectively providing rapid and long-lasting interventions.[1] In previous studies, we have shown that light-stimulated LCEs can mimic muscular function and potentiate cardiac contraction. However, their integration with light sources has not been explored so far.[16] Here, a prototype of a BCU was designed and developed

thus allowing us to demonstrate that light power can be converted into mechanical work in an integrated mLED-LCE system. Thanks to the patterned illumination provided by the mLED array, the BCU performance (in terms of both force amplitude and kinetics) can be fine-tuned in the attempt of reproducing the physiological behaviors of native muscle.

4. Experimental Section

Film Preparation: Material preparation followed a previously reported methodology that is briefly described here (Figure 2).[9,11,27] The composition of the monomer mixture and the chemical structures of the reagents are reported in Figure 1c. RM257 and C6BP are LC reactive mesogens; the former is a diacrylate crosslinker, while the latter is a polymerizable mesogen with one acrylate end. Disperse Red 1 Acrylate is a polymerizable dye. Irgacure 369 is a UV-responsive photoinitiator to trigger radical polymerization. RM257 was purchased from Wilshire Technologies, C6BP was purchased from Synthon Chemicals GmbH, Disperse Red 1 Acrylate was supplied by Specific Polymers, Irgacure 369 was purchased from Sigma Aldrich. All reagents are solid and were used without any further purification. The monomeric mixture contained 88% mol/mol C6BP, 10% mol/mol RM257, 1% mol/mol DR1 Acrylate and 1% mol/mol Irgacure 369 photoinitiator. Figure S4 (Supporting Information) reports characterization with the polarized optical microscopy of the monomer mixture and the LC network in terms of mesophase behavior and alignment. LC cells were fabricated using two glass slides coated with PVA. These substrates were rubbed uniaxially with a velvet cloth to force homogeneous planar alignment of LC monomers. After rubbing, slides were glued together, using silica beads as spacer, to guarantee a thickness of 10 μm. The mixture was infiltrated in the hollow space between the glass slides by capillarity in its isotropic phase (at 75 °C). Temperature was then decreased to 45 °C, and cells were irradiated with a UV lamp at 385 nm for 10 min (M385L2-C4, Thorlabs) to polymerize the mixture. A post-curing step, by irradiating the samples with UV light for 10 min at 65 °C, was carried out afterward. Cells were immersed in water and opened manually to detach the LCE film.

Mini-LED Array Assembly and Characterization: Blue mLEDs (150040BS73220, Würth Elektronic, Germany) were mounted on a custom-made printed circuit board following the geometry described in Figure 3a. Each mLED was independently driven at constant current (maximum driving current of 20 mA) by a custom-made 16-channel driver. Light power provided by each mLED was measured by using a power meter (PD300-3W, Ophir Photonics Group, Germany) located as close as possible to mLED die. In accordance with the scheme of fabrication of the biomimetic contractile unit (BCU), the light intensity profile of mLEDs was monitored by using a CMOS camera (340M-GE, Thorlabs, Germany) after placing a sensor at the distance of 0.2 mm from the mLEDs.

Mechanical Measurements: LCE films were cut into strips, following rubbing direction, whose dimensions were ≈8 mm length × 0.75 mm width. Samples were mounted between the platinum end of a force transducer (KG4A, Scientific Instruments Heidelberg, Germany) on top and an afterload below. Measurements were performed in air at room temperature. A custom-made LabVIEW software was used for force signal recording. Maximal active force was evaluated when the force reached a steady-state plateau while the kinetics of force development were assessed by measuring the half time of force rise and decay. Under isotonic contractions, the LCE strip displacement was monitored with a CMOS camera (340M-GE, Thorlabs, Germany). The shortening velocity was evaluated by measuring the relative displacement value of the LCE strip after applying different afterloads.

Supporting Information

Supporting Information is available from the Wiley Online Library or from the author.

Acknowledgements

G.V. and B.G. contributed equally to this work. The authors thank Simone Donato e Marta Rojas for the help in preparing LCE films. This work was financially supported by the European Union's Horizon 2020 research and innovation programme under grant agreement No 952166 (REPAIR). The authors thank MIUR-Italy ("Progetto Dipartimenti di Eccellenza 2018–2022" for the funds allocated to the Department of Chemistry "Ugo Schiff", and to the Department of Experimental and Clinical Medicine).

Open Access Funding provided by Universita degli Studi di Firenze within the CRUI-CARE Agreement.

Conflict of Interest

The authors declare no conflict of interest.

Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Keywords

artificial muscles, contractile units, liquid crystal elastomers, mini-LEDs, smart materials

Received: March 16, 2022
Revised: May 2, 2022
Published online:

[1] J. Han, D. Trumble, *Bioengineering* **2019**, *6*, 18.
[2] M. Radisic, K. L. Christman, *Mayo Clin. Proc.* **2013**, *88*, 884.
[3] S. Coyle, C. Majidi, P. Leduc, K. J Hsia, *Extreme Mech. Lett.* **2018**, *22*, 51.
[4] S. M. Mirvakili, I. W. Hunter, *Adv. Mater.* **2018**, *30*, 1704407.
[5] P.-G. De Gennes, M. Hébert, R. Kant, *Macromol. Symp.* **1997**, *113*, 39.
[6] D. Broer, G. P. Crawford, S. Zumer, eds. *Cross-Linked Liquid Crystalline Systems: From Rigid Polymer Networks to Elastomers*, CRC Press, Boca Raton, Florida **2011**.
[7] T. J. White, D. J. Broer, *Nat. Mater.* **2015**, *14*, 1087.
[8] S. W. Ula, N. A. Traugutt, R. H. Volpe, R. R. Patel, K. Yu, C. M. Yakacki, *Liq. Cryst. Rev.* **2018**, *6*, 78.
[9] R. S. Kularatne, H. Kim, J. M. Boothby, T. H. Ware, *J. Polym. Sci., Part B: Polym. Phys.* **2017**, *55*, 395.
[10] M. Warner, E. M. Terentjev, *Liquid Crystal Elastomers*, Oxford University Press, Oxford, **2007**.
[11] D. Martella, D. Antonioli, S. Nocentini, D. S. Wiersma, G. Galli, M. Laus, C. Parmeggiani, *RSC Adv.* **2017**, *7*, 19940.
[12] J. M. Mccracken, B. R. Donovan, K. M. Lynch, T. J. White, *Adv. Funct. Mater.* **2021**, *31*, 2100564.
[13] D. Martella, S. Nocentini, D. Antonioli, M. Laus, D. S. Wiersma, C. Parmeggiani, *Polymers* **2019**, *11*, 1644.
[14] R. K. Shaha, D. R. Merkel, M. P. Anderson, E. J. Devereaux, R. R. Patel, A. H. Torbati, N. Willett, C. M. Yakacki, C. P. Frick, *J. Mech. Behav. Biomed. Mater.* **2020**, *107*, 103757.
[15] D. L. Thomsen, P. Keller, J. Naciri, R. Pink, H. Jeon, D. Shenoy, B. R. Ratna, *Macromolecules* **2001**, *34*, 5868.
[16] C. Ferrantini, J. M. Pioner, D. Martella, R. Coppini, N. Piroddi, P. Paoli, M. Calamai, F. S. Pavone, D. S. Wiersma, C. Tesi, E. Cerbai, C. Poggesi, L. Sacconi, C. Parmeggiani, *Circ. Res.* **2019**, *124*, e44.

[17] D. M. Bers, *Excitation-Contraction Coupling and Cardiac Contractile Force*, Springer Netherlands, Dordrecht, **2001**.
[18] H. Zeng, O. M. Wani, P. Wasylczyk, A. Priimagi, *Macromol. Rapid Commun.* **2018**, *39*, 1700224.
[19] H. Zeng, P. Wasylczyk, C. Parmeggiani, D. Martella, M. Burresi, D. S. Wiersma, *Adv. Mater.* **2015**, *27*, 3883.
[20] M. Pozo, L. Liu, M. Pilz Da Cunha, D. J. Broer, A. P. H. J. Schenning, *Adv. Funct. Mater.* **2020**, *30*, 2005560.
[21] M. D. Pozo, J. A. H. P. Sol, S. H. P. Van Uden, A. R. Peeketi, S. J. D. Lugger, R. K. Annabattula, A. P. H. J. Schenning, M. G. Debije, *ACS Appl. Mater. Interfaces* **2021**, *13*, 59381.
[22] O. M. Wani, H. Zeng, A. Priimagi, *Nat. Commun.* **2017**, *8*, 15546.
[23] D. Martella, S. Nocentini, D. Nuzhdin, C. Parmeggiani, D. S. Wiersma, *Adv. Mater.* **2017**, *29*, 1704047.
[24] M. Yamada, M. Kondo, J.-I. Mamiya, Y. Yu, M. Kinoshita, C. J. Barrett, T. Ikeda, *Angew. Chem.* **2008**, *120*, 5064.
[25] M. Zmyślony, K. Dradrach, J. Haberko, P. Nałęcz-Jawecki, M. Rogóż, P. Wasylczyk, *Adv. Mater.* **2020**, *32*, 2002779.
[26] A. S. Kuenstler, H. Kim, R. C. Hayward, *Adv. Mater.* **2019**, *31*, 1901216.
[27] D. Liu, D. J. Broer, *Langmuir* **2014**, *30*, 13499.
[28] D. Martella, S. Nocentini, C. Parmeggiani, D. S. Wiersma, *Faraday Discuss.* **2020**, *223*, 216.
[29] C. Holubarsch, *Cardiovasc. Res.* **1998**, *37*, 46.
[30] L. Larsson, R. L. Moss, *J. Physiol.* **1993**, *472*, 595.
[31] N. El-Atab, R. B. Mishra, F. Al-Modaf, L. Joharji, A. A. Alsharif, H. Alamoudi, M. Diaz, N. Qaiser, M. M. Hussain, *Adv. Intell. Syst.* **2020**, *2*, 2000128.
[32] A. Kirillova, L. Ionov, *J. Mater. Chem. B* **2019**, *7*, 1597.
[33] R. Sarvari, P. Keyhanvar, S. Agbolaghi, M. S. Gholami Farashah, A. Sadrhaghighi, M. Nouri, L. Roshangar, *Int. J. Polym. Mater. Polym. Biomater.* **2022**, *71*, 315.
[34] T. H. Ware, M. E. Mcconney, J. J. Wie, V. P. Tondiglia, T. J. White, *Science* **2015**, *347*, 982.
[35] T. H. Ware, T. J. White, *Polym. Chem.* **2015**, *6*, 4835.
[36] T. Guin, H. E. Hinton, E. Burgeson, C. C. Bowland, L. T. Kearney, Y. Li, I. Ivanov, N. A. Nguyen, A. K. Naskar, *Adv. Intell. Syst.* **2020**, *2*, 2000022.
[37] T. Guin, M. J. Settle, B. A. Kowalski, A. D. Auguste, R. V. Beblo, G. W. Reich, T. J. White, *Nat. Commun.* **2018**, *9*, 2531.
[38] R. Coppini, C. Ferrantini, L. Yao, P. Fan, M. Del Lungo, F. Stillitano, L. Sartiani, B. Tosi, S. Suffredini, C. Tesi, M. Yacoub, I. Olivotto, L. Belardinelli, C. Poggesi, E. Cerbai, A. Mugelli, *Circulation* **2013**, *127*, 575.

