

DEFECT PAIRS IN NEMATIC CELL ALIGNMENT ON DOUBLY CONNECTED DOMAINS

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ABSTRACT. We consider the orientational order that arises from the alignment of anisotropic biological cells confined in bounded domains. Especially, it is known that topological defects, where the orientation angles are not well-defined, play an important role in the global pattern formation of cell alignment. Hence, it is important to investigate the relationship between the shape of the region and the location of the defects. The orientational order of cells is theoretically modeled as a harmonic function achieving the minimum elastic energy state of the nematic liquid crystal, and an analytical formula in simply connected domains is given by Miyazako and Nara [1]. In this paper, we extended this study to construct an analytic formula of cell angle in the doubly connected domains, where topological defects and boundary shapes are represented as the positions of logarithmic singularities and as conformal maps from a given region to a standard annular region respectively. In addition, using this analytical formula, we propose a numerical algorithm to minimize elastic energy, from which we investigate cell alignment in doubly connected domains with anisotropic quadrilateral boundaries. Our numerical simulations suggest that pairs of topological defects tend to be located around corners of the boundaries, which will be a design principle of the boundary geometry for controlling the defect positions and cell alignment.

1. INTRODUCTION

Biological cells making up muscle and epithelial tissues become spindle-shaped as the number of cells increases, and they are thus likely to acquire the orientational order by aligning in a specific direction. For instance, filamentous cytoskeletal proteins in a cell have a locally preferred orientation, and it thus determines the shape of the cell and controls the direction of its movement. Recently, there has been a growing number of research works revealing how such orientational orders in various biological organisms affect biological phenomena by using theoretical models of nematic liquid crystals [2, 3]. In particular, we have significant interests in singular points in the domain at which the orientation angles of cells cannot be defined, which are referred to as *topological defects*. Since the orientational angle of cells in the neighborhood of a topological defect is not well-aligned, it gives rise to force imbalance among surrounding cells. As a result, it yields the deformations of cell populations such as aggregation [4] and extrusion [5, 6]. It is also found that the movement of these topological defects induces complex flow phenomena [7], which are called *active nematics*. Active nematics are now intensively investigated in the fields of non-equilibrium statistical physics as well as biophysics.

Key words and phrases. nematic liquid crystals, topological defect, complex analysis, conformal mapping.

With the development of research on active nematics, there emerges a technological interest in bioengineering for regulating the orientation structures and the movement of topological defects in order to improve the reproducibility in experiments [8, 9, 10, 11]. One of the main experimental strategies to control topological defects is confining cells and biomolecules in closed domains or channels with various geometric features such as punctured holes and utilizing the intrinsic orientation of cells and biomolecules along the boundaries of domains.

The behavior of the defect locations has been investigated for specific simply connected domains such as cylindrical grooves [12], cylindrical particles, and parabolic cylinders [13]. Miyazako and Nara [1] derived an analytic formula for the orientation angle of nematic liquid crystals in a unit circle, thereby constructing successfully a general formula for simply connected domains with conformal mapping. Chandler and Spagnolie also used complex functions to derive analytic solutions for calculating nematic order with an immersed body and considered the existence of the topological defects on the surface of the body [14]. The next simplest shape of domains with non-trivial geometric features is concentric annuli. In the fields of biophysics and soft matter, the nematic alignment on concentric annuli has been considered to achieve periodic boundary conditions [15] and to change topological constraints of the alignment [16]. However, despite its geometric simplicity and importance, theoretical investigations of topological defects of nematic liquid crystals in annular regions are still developing. For instance, Gârlea et al. [16] have conducted a Monte Carlo simulation minimizing the elastic energy of liquid crystals. When the inner circle radius of the annulus is small, they found that there is a pair of topological defects, one is near the inner boundary and the other is the outer boundary. They experimentally observe the orientation of a rod-shaped *fd*-virus encapsulated in an annular chamber, finding a pattern of topological defects similar to that obtained in their simulation.

Manyuhina et al. [17] and Lewis et al. [18] have investigated the effect of topological defects near the boundary of the annulus region theoretically. They assume that the size of the liquid crystals is ignorable, the orientation angle changes continuously and the scalar order parameter representing the degree of orientation is constant. They then consider the Frank-Oseen elastic energy, which is elastic energy derived from the orientation of liquid crystals, and approximate it with a well-known method called the one-constant approximation in the liquid crystal theory [19]. Taking the variation of the elastic energy, they showed that the orientation angle is to be harmonic. Hence, by expressing the orientation angle around the topological defect as a harmonic function, they evaluated the approximate elastic energy analytically and discussed an energetically stable orientation pattern. However, since the topological defects are fixed on the boundaries of the annulus in these studies, it is not possible to predict the locations of the energy-minimizing patterns with topological defects inside the annulus.

All previous studies described above have focused on concentric annuli. We have not yet conducted a systematic investigation of the energy-minimizing patterns when the shapes of the inner and outer boundaries are deformed. Hence, in order to investigate the influence of the geometry of domains on the generation of topological defects, it is necessary to construct an analytic model expressing the orientation angle of cells in doubly connected domains with boundaries having arbitrary shapes. In addition, from the viewpoint of the applications to biological problems, it is

necessary to examine the behavior of topological defects under boundary conditions, called strong anchoring, where the orientation angle is tangent to the boundary [20, 21].

The present paper aims to provide an explicit analytic formula that describes the orientation angle of nematic liquid crystals in doubly connected domains, thereby predicting the locations of topological defects when the shape of boundaries is given. We utilize the theory of complex functions as our mathematical approach since the orientation angle is modeled by a harmonic function. In this paper, we take the same approach as Miyazako and Nara [1] to the case of doubly connected domains using a transcendental function called the Schottky-Klein-Prime (SKP) function [22, 23]. It is noted that the SKP function was also used in Chandler and Spagnolie's study, which considered concentric annuli to derive an analytic solution of nematic order with multiple immersed bodies [24]; however, they considered the existence of the defects on the surface of the bodies. Compared to this study [24], **our analytic formulae allow defects to exist in any place inside doubly connected domains, and do not have limitations on the number of defects.**

The paper is constructed as follows. In Section 2, we review a mathematical model of cell alignments based on the theory of nematic liquid crystals and characterize the orientation angles of the cells as a minimizer of the Frank elastic energy. In Section 3, we provide an analytic formula for cell alignment in concentric annuli using the SKP function. It is then extended to the analytic formula for general doubly connected domains with the method of conformal mappings. In addition, based on the analytic formula, we also develop a numerical procedure for finding the configurations of topological defects that minimize the Frank elastic energy. In Section 4, after verifying that the numerical procedure works well for the topological defects in concentric annuli, we observe the energy-minimizing configurations in doubly connected domains with four corners in order to discuss how the shape of the boundary affects the locations of the topological defects. We conclude the results in the last section.

2. MATHEMATICAL MODEL OF CELL ALIGNMENTS

The cell alignment of biological organisms has been effectively modeled by the theory of nematic liquid crystals [19]. **Figure 1 shows the problem setup for calculating the cell alignment in a doubly connected domain.** Let us consider a doubly connected domain Ω whose outer and inner boundaries, say $\partial\Omega_1$ and $\partial\Omega_2$ respectively, are Jordan curves. Suppose also that the domain Ω is filled with nematic liquid crystals whose size is negligibly small. The orientational direction of the nematic liquid crystals is then represented by a continuous function $\mathbf{n} = [\cos \phi(x, y), \sin \phi(x, y)]^T$. Since the nematic liquid crystals are non-polar molecules, we identify the angle $\mathbf{n}$ with $-\mathbf{n}$. That is to say, the two angles $\phi_1(x, y)$, and $\phi_2(x, y)$ are equivalent if there exists an integer $n \in \mathbb{Z}$ such that $\phi_1(x, y) = \phi_2(x, y) + n\pi$ holds for any $(x, y) \in \Omega$.

The distortion of the orientational change inside the domain Ω yields elasticity. We here suppose the existence of a finite number of singular points where $\nabla\phi(x, y)$ are not well-defined. With the one-constant approximation in the liquid crystal theory [19], the elastic energy of the nematic liquid crystals, called the Frank elastic energy is then given by

$$(1) \quad F = \frac{K}{2} \iint_{\tilde{\Omega}} |\nabla\phi(x, y)|^2 dx dy,$$

in which $\tilde{\Omega}$ is a punctured domain obtained by removing the singular points from Ω . As discussed in [1], the orientational angle for the nematic liquid crystals is physically characterized as the minimizer of the Frank elastic energy. Hence, the orientational angle ϕ satisfies $\nabla^2 \phi(x, y) = 0$, which means that it is a harmonic function on $\tilde{\Omega}$. As the boundary condition on $\partial\Omega_1$ and $\partial\Omega_2$, we assume that the orientation angle of the nematic liquid crystals is tangent to the boundaries.

We now characterize the singular points more clearly and provide a topological constraint on them. In this paper, we consider the defects as point-like objects whose singularities are expressed by complex logarithmic functions in a conventional manner [19]. Let $(x_0, y_0) \in \Omega$ be the location of a singular point where the orientation angle $\phi(x, y)$ is not well-defined. If there exists a half-integer q such that $\oint_C \frac{\partial \phi}{\partial s} ds = 2\pi q$ holds for an arbitrary closed curve C containing no singular points inside except for (x_0, y_0) , the singular point is called the topological defect with topological charge q . In this paper, we assume that there are N topological defects with topological charge q_k , $k = 1, \dots, N$. By D_k , we denote a closed domain enclosing the k th topological defect only. Then it follows from Green's theorem and $\nabla^2 \phi = 0$ on $\Omega \setminus \bigcup_{k=1}^N D_k$ that we have

$$(2) \quad \oint_{\partial\Omega_1} \frac{\partial \phi}{\partial s} ds - \oint_{\partial\Omega_2} \frac{\partial \phi}{\partial s} ds - \sum_{k=1}^N \oint_{\partial D_k} \frac{\partial \phi}{\partial s} ds = 0.$$

Owing to the tangential boundary condition for ϕ along the boundaries $\partial\Omega_1$ and $\partial\Omega_2$, we have $\oint_{\partial\Omega_1} \frac{\partial \phi}{\partial s} ds = \oint_{\partial\Omega_2} \frac{\partial \phi}{\partial s} ds = 2\pi$. Hence, the equation (2) yields the following constraint on the topological charges.

$$(3) \quad \sum_{k=1}^N q_k = 0.$$

It is noted that this topological constraint is different from that for simply connected domains. In more detail, the summation of the topological charges should be equal to $+1$ in the case of simply connected domains [1], which indicates the existence of the defects is inevitable. On the contrary, the defects do not necessarily exist in doubly connected domains. Under this topological constraint, we need to obtain a harmonic function $\phi(x, y)$ in Ω satisfying the tangential boundary condition on $\partial\Omega_1$ and $\partial\Omega_2$.

3. ANALYTIC FORMULAE OF CELL ALIGNMENT

In this section, we derive analytic formulae for cell alignment in doubly connected domains and propose a prediction method for detecting stable defect configurations, as shown in Figure 2. We first derive an analytic formula for cell alignment in concentric annuli (Step 1), which is then extended to the analytic formula for doubly connected domains with the method of conformal mappings (Step 2). Since the derived formulae are functions of defect positions, we cannot determine the most stable configuration of the topological defect positions only by the derived formulae. Thus, we finally develop a numerical minimization algorithm for determining the configurations of topological defects that minimize the Frank elastic energy (Step 3).

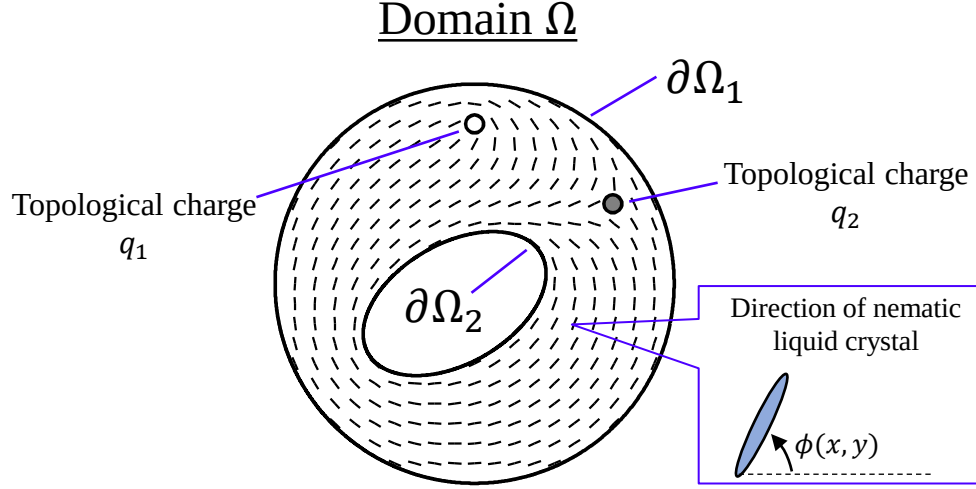


FIGURE 1. Schematic of the problem setup for calculating the cell alignment in a doubly connected domain. In this figure, there are $N = 2$ topological defects with the topological charge of $q_1 = +1/2$ and $q_2 = -1/2$.

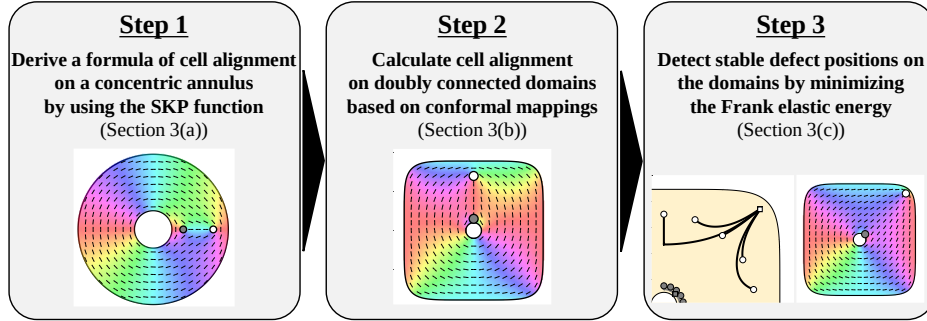


FIGURE 2. A prediction method for detecting stable defect configurations proposed in Section 3.

3.1. Analytic formula for canonical annuli. Let $\mathcal{D}$ be a concentric annulus in the complex ζ -plane as follows.

$$\mathcal{D} = \{\zeta \in \mathbb{C} \mid \rho < |\zeta| \leq 1\},$$

in which $0 < \rho < 1$ denotes the modulus of the domain. For a given ρ and $\alpha \in \mathcal{D}$, we introduce the following functions.

(4)

$$P(\zeta) = (1-\zeta) \prod_{\ell=1}^{\infty} (1-\rho^{2\ell}\zeta)(1-\rho^{2\ell}/\zeta), \quad \omega(\zeta, \alpha) = -\frac{\alpha}{C^2} P(\zeta/\alpha), \quad C = \prod_{n=1}^{\infty} (1-\rho^{2n}).$$

The function $\omega(\zeta, \alpha)$ is called the Schottky Klein prime function associated with the domain $\mathcal{D}$, in which the infinite product converges rapidly owing to $\rho \in (0, 1)$. **See [23] for details about this function.** The function $\omega(\zeta, \alpha)$ has zeros at $\zeta = \rho^{2\ell}\alpha$ for $\ell \in \mathbb{Z}$ in the complex ζ -plane, but there is only one zero at $\zeta = \alpha$ when the domain is restricted to $\mathcal{D}$.

Suppose that there exist N defects at $z_k \in \mathcal{D}$, i.e., $\rho < |z_k| < 1$, with topological charges $q_k \in \mathbb{R}$ of half integers for $k = 1, \dots, N$. Then the set of the defects is defined by $\mathcal{Z} = \{z_1, z_2, \dots, z_N\}$. For any $n \in \mathbb{Z}$, with the polar coordinate representation $z_k = r_k e^{i\theta_k}$ of the defect locations, we introduce a real constant Q_n as follows.

$$(5) \quad Q_n = n\pi + \sum_{k=1}^N q_k(\theta_k + \pi).$$

Suppose now that the function $f_{\mathcal{D}}(\zeta; \mathcal{Z})$ on $\mathcal{D} \subset \mathcal{Z}$ is defined by

$$(6) \quad f_{\mathcal{D}}(\zeta; \mathcal{Z}) = - \sum_{k=1}^N i q_k [\log \omega(\zeta, z_k) + \log \omega(\zeta, 1/\bar{z}_k) + \log(-\bar{z}_k)] - i \log \zeta - Q_n \frac{\log \zeta}{\log \rho} - \frac{\pi}{2},$$

in which $\bar{z}$ denotes the complex conjugate of $z \in \mathbb{C}$. Then the function

$$(7) \quad \phi_{\mathcal{D}}(x, y; \mathcal{Z}) = \operatorname{Re} [f_{\mathcal{D}}(\zeta; \mathcal{Z})]$$

gives rise to an analytic formula of the cell alignment at $\zeta = x + iy$ on $\mathcal{D}$.

Proposition 1. *The function $\phi_{\mathcal{D}}(x, y; \mathcal{Z})$ satisfies the following three conditions.*

- (I) $\phi_{\mathcal{D}}(x, y; \mathcal{Z})$ is harmonic on $\mathcal{D} \setminus \mathcal{Z}$;
- (II) For any bounded connected domains D_k containing z_k only,

$$\oint_{\partial D_k} \frac{\partial \phi_{\mathcal{D}}}{\partial s} ds = 2\pi q_k;$$

- (III) The function $\hat{\phi}_{\mathcal{D}}(x, y) = \phi_{\mathcal{D}}(x, y; \mathcal{Z})/(\pi\mathbb{Z}) \simeq (-\pi/2, \pi/2]$ satisfies the boundary condition $\hat{\phi}_{\mathcal{D}}(\zeta) = \theta - \frac{\pi}{2}$ on the boundaries $\zeta = e^{i\theta}$ and $\zeta = \rho e^{i\theta}$ of the annulus $\mathcal{D}$.

Proof. The first condition is obvious since the logarithmic function is harmonic on $\mathcal{D} \setminus \mathcal{Z}$. The functions $\omega(\zeta, 1/\bar{z}_k)$ and $\log \zeta$ is holomorphic, and the function $\omega(\zeta, z_k) \sim (\zeta - z_k)$ in the neighborhood of $\zeta = z_k$ on $\mathcal{D}$. Hence, the second condition holds by the residue theorem. The third boundary condition is confirmed as follows. Let us consider the first term of (6). In the quotient space $\mathbb{R}/(\pi\mathbb{Z})$, we have

$$\log[-z_k/C^2 P(\zeta/z_k)] + \log[-1/(C^2 \bar{z}_k) P(\zeta \bar{z}_k)] + \log(-\bar{z}_k) = \log[(-z_k) P(\zeta/z_k) P(\zeta \bar{z}_k)] - 4 \log C,$$

in which

$$(8) \quad -z_k P(\zeta/z_k) P(\zeta \bar{z}_k) = (\zeta - z_k)(1 - \zeta \bar{z}_k) \prod_{\ell=1}^{\infty} (1 - \rho^{2\ell} \zeta/z_k)(1 - \rho^{2\ell} z_k/\zeta)(1 - \rho^{2\ell} \zeta \bar{z}_k)(1 - \rho^{2\ell}/(\zeta \bar{z}_k)),$$

owing to (4). Evaluating (8) at the boundary $\zeta = e^{i\theta}$, we obtain

$$\begin{aligned} & (e^{i\theta} - z_k)(1 - e^{i\theta}\bar{z}_k) \prod_{\ell=1}^{\infty} (1 - \rho^{2\ell}e^{i\theta}/z_k)(1 - \rho^{2\ell}z_k/e^{i\theta})(1 - \rho^{2\ell}e^{i\theta}\bar{z}_k)(1 - \rho^{2\ell}/(e^{i\theta}\bar{z}_k)) \\ &= e^{i\theta}(1 - e^{-i\theta}z_k)(1 - e^{i\theta}\bar{z}_k) \prod_{\ell=1}^{\infty} (1 - \rho^{2\ell}e^{i\theta}/z_k)(1 - \rho^{2\ell}e^{-i\theta}z_k)(1 - \rho^{2\ell}e^{i\theta}\bar{z}_k)(1 - \rho^{2\ell}e^{-i\theta}/\bar{z}_k). \end{aligned}$$

Acting $-iq_k \log$ on this formula and taking its real part, we have $q_k\theta$. Summing this term with respect to k yields $\sum_{k=1}^N q_k\theta = 0$ owing to (3). Regarding the remaining parts of (6), it follows from $\text{Re}[-i \log e^{i\theta}] = \theta$ and $\text{Re}[\log e^{i\theta}] = 0$ that $\hat{\phi}_{\mathcal{D}}(\zeta) = \theta - \pi/2$ on $|\zeta| = 1$ as desired.

Substituting $\zeta = \rho e^{i\theta}$ into (8), we have

$$\begin{aligned} & (\rho e^{i\theta} - z_k)(1 - \rho e^{i\theta}\bar{z}_k) \prod_{\ell=1}^{\infty} (1 - \rho^{2\ell+1}e^{i\theta}/z_k)(1 - \rho^{2\ell-1}z_k/e^{i\theta})(1 - \rho^{2\ell+1}e^{i\theta}\bar{z}_k)(1 - \rho^{2\ell-1}/(e^{i\theta}\bar{z}_k)) \\ &= (\rho e^{i\theta} - z_k)(1 - \rho e^{i\theta}\bar{z}_k)(1 - \rho^3e^{i\theta}/z_k)(1 - \rho^5e^{i\theta}/z_k) \cdots (1 - \rho e^{-i\theta}z_k)(1 - \rho^3e^{-i\theta}z_k)(1 - \rho^5e^{-i\theta}z_k) \\ & \quad \cdots (1 - \rho^3e^{i\theta}\bar{z}_k)(1 - \rho^5e^{i\theta}\bar{z}_k) \cdots (1 - \rho e^{-i\theta}/\bar{z}_k)(1 - \rho^3e^{-i\theta}/\bar{z}_k)(1 - \rho^5e^{-i\theta}/\bar{z}_k) \cdots. \end{aligned}$$

The real parts of the logarithm of the pairs $(1 - \rho^k e^{i\theta}\bar{z}_k)(1 - \rho^k e^{-i\theta}z_k)$ for $k \geq 1$ and $(1 - \rho^k e^{i\theta}/z_k)(1 - \rho^k e^{-i\theta}/\bar{z}_k)$ for $k \geq 3$ vanish. The remaining part is given by

$$-iq_k \log [(\rho e^{i\theta} - z_k)(1 - \rho e^{-i\theta}/\bar{z}_k)] = -iq_k \log [-z_k(1 - \rho e^{i\theta}/z_k)(1 - \rho e^{-i\theta}/\bar{z}_k)].$$

The real part then becomes $q_k \text{Im}[\log(-z_k)] = q_k(\theta_k + \pi)$ owing to $z_k = r_k e^{i\theta_k}$. Hence, the real part of the first term of (6) is equivalent to Q_0 . In addition, since $\text{Re}[-i \log \rho e^{i\theta}] = \theta$ and $\text{Re}[-Q_n(\log \rho e^{i\theta}/\log \rho)] = -Q_n = -Q_0 - n\pi$, we have $\hat{\phi}_{\mathcal{D}}(\zeta) = \theta - \pi/2$ on the inner boundary $|\zeta| = \rho$ in the quotient space $\mathbb{R}/\pi\mathbb{Z}$. $\square$

We show some numerical examples of $\hat{\phi}_{\mathcal{D}}(x, y; \mathcal{Z})$ when two defects with the topological charges $\pm 1/2$ exist on the annulus $\mathcal{D}$ with the modulus $\rho = 0.25$. The free parameter in (6) is chosen by $Q_n = Q_0$. Figure 3 shows the patterns of the cell alignment on the annulus for various z_1 and z_2 . Each panel shows that the alignment angle of the cells agrees with the tangent direction of the boundaries of the annulus $\mathcal{D}$, satisfying the boundary condition.

Figure 4 shows the cell alignments for two defects on the annulus $\mathcal{D}$ of the modulus $\rho = 0.1$. In panels (a) and (b), the defects with the topological charge $q_1 = +1/2$ and $q_2 = -1/2$ are at the same locations $z_1 = 0.5e^{i\frac{\pi}{3}}$ and $z_2 = 0.5e^{-i\frac{\pi}{3}}$ but the free parameters are Q_0 and Q_{-1} respectively. They indicate that different patterns of the cell alignment are obtained when we choose the other $Q_n \neq Q_0$, even if the locations are the defects remain the same. On the other hand, in panels (c) and (d), the two defects are located at $\tilde{z}_1 = 0.5e^{i\frac{2\pi}{3}} = -\bar{z}_1$ and $\tilde{z}_2 = 0.5e^{-i\frac{2\pi}{3}} = -\bar{z}_2$, which are symmetric with the defects of panels (a) and (b) about the imaginary axis. We notice that the cell alignments do not inherit the symmetry of the defect locations. In the meantime, we observe that the cell alignment of the panel (b) is symmetric with the pattern of the panel (c). This means that the derived formula (6) is not unique for given defect positions. Thus, another criterion to determine Q_n is required from the physical point of view since n is the free parameter in the formula (6). It is noted that this non-uniqueness problem was also mentioned in

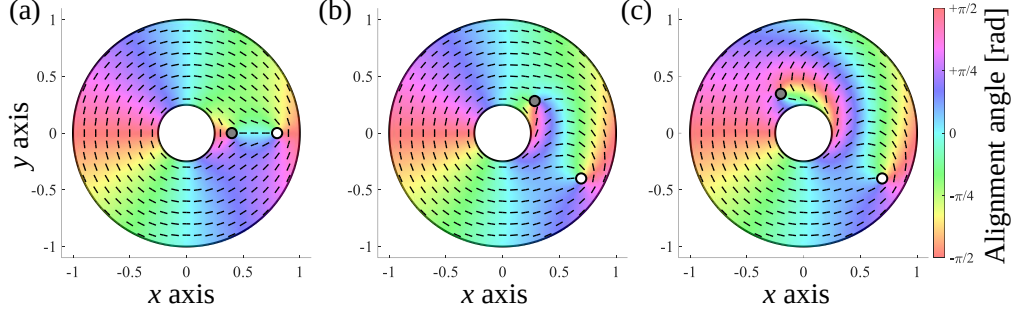


FIGURE 3. Cell alignments in the annulus $\mathcal{D}$ with $\rho = 0.25$. The white and the gray circles represent the defects with the topological charge $+1/2$ and $-1/2$ respectively. The color plot represents the angle in $[-\pi/2, \pi/2]$. The locations of the defects are given by (a) $z_1 = 0.8$, $z_2 = 0.4$; (b) $z_1 = 0.8e^{-i\pi/6}$, $z_2 = 0.4e^{+i\pi/4}$; (c) $z_1 = 0.8e^{-i\pi/6}$, $z_2 = 0.4e^{i2\pi/3}$.

Chandler and Spagnolie's study [24], and the free parameter n is related to the “period” in their study.

3.2. Analytic formula for doubly connected domains. From (7), we derive the analytic formula for the cell alignment on a given doubly connected domain $\mathcal{D}_w$ in the complex w -plane. Let $w = g(\zeta)$ denote the conformal mapping from the canonical annulus $\mathcal{D}$ to the target domain $\mathcal{D}_w$. The outer and the inner boundaries of $\mathcal{D}_w$ are parameterized by $w_1(\theta) = g(e^{i\theta}) = u_1(\theta) + iv_1(\theta)$ and $w_2(\theta) = g(pe^{i\theta}) = u_2(\theta) + iv_2(\theta)$ for $\theta \in [0, 2\pi)$ respectively. Then, the angles $\nu_i(\theta)$ of the tangent direction of the outer and the inner boundaries are represented by

$$(9) \quad \nu_i(\theta) = \arctan \frac{\dot{v}_i(\theta)}{\dot{u}_i(\theta)},$$

where $\dot{u}_i(\theta) = \frac{du_i}{d\theta}$ and $\dot{v}_i(\theta) = \frac{dv_i}{d\theta}$. We assume that the angle of the cell alignment is equivalent to $\nu_i(\theta)$ at each boundary of $\mathcal{D}_w$, which is the boundary condition of the analytic formula given as follows.

Proposition 2. *Suppose that N defects with the topological charge q_k satisfying (3) are located at w_k on the domain $\mathcal{D}_w$ for $k = 1, 2, \dots, N$. Let the set of the defects on $\mathcal{D}_w$ and $\mathcal{D}$ be denoted by $\mathcal{W} = \{w_1, \dots, w_N\}$ and $\mathcal{Z}^* = \{z_k = g^{-1}(w_k) \mid k = 1, \dots, N\}$ respectively. The function $f_{\mathcal{D}_w}$ on $\mathcal{D}_w \setminus \mathcal{W}$ is defined by*

$$(10) \quad f_{\mathcal{D}_w}(w; \mathcal{W}) = f_{\mathcal{D}}(g^{-1}(w); \mathcal{Z}^*) - i \log g'(g^{-1}(w)).$$

Then, $\phi_{\mathcal{D}_w}(u, v; \mathcal{W}) \equiv \text{Re}[f_{\mathcal{D}_w}(w; \mathcal{W})]$ satisfies the following three conditions.

- (i) $\phi_{\mathcal{D}_w}(u, v; \mathcal{W})$ is harmonic on $\mathcal{D}_w \setminus \mathcal{W}$;
- (ii) For any bounded connected domain D_k containing w_k only,

$$\oint_{\partial D_k} \frac{\partial \phi_{\mathcal{D}_w}}{\partial s} ds = 2\pi q_k;$$

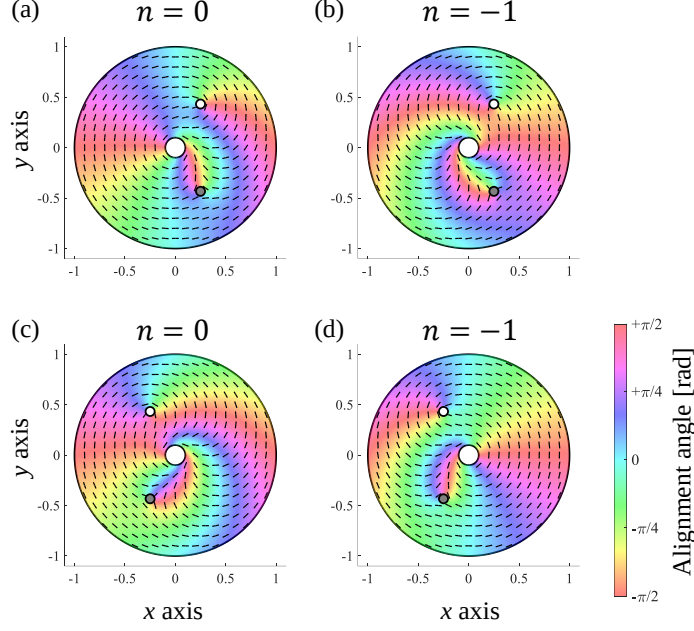


FIGURE 4. Cell alignments on the annulus $\mathcal{D}$ of the modulus $\rho = 0.1$ for different z_1, z_2 and Q_n . The white and the gray circles represent the defects with the topological charges $\pm 1/2$ respectively. (a) The locations of the defects are $z_1 = 0.5e^{-i\frac{\pi}{3}}$ and $z_2 = 0.5e^{i\frac{\pi}{3}}$ with $Q_n = Q_0$. (b) The locations of the defects are the same as the panel (a), but $Q_n = Q_{-1}$. (c) The locations of the defects are $\tilde{z}_1 = 0.5e^{i\frac{2\pi}{3}} (= -\bar{z}_1)$ and $\tilde{z}_2 = 0.5e^{-i\frac{2\pi}{3}} (= -\bar{z}_2)$ with $Q_n = Q_0$. (d) The locations of the defects are the same as the panel (c), but $Q_n = Q_{-1}$.

- (iii) $\hat{\phi}(u, v) = \phi_{\mathcal{D}_w}(u, v; \mathcal{W})/(\pi\mathbb{Z}) \simeq (-\pi/2, \pi/2]$ satisfies $\hat{\phi}(w_1(\theta)) = \nu_1(\theta)$ on the outer boundary $w = w_1(\theta)$ and $\hat{\phi}(w_2(\theta)) = \nu_2(\theta)$ on the inner boundary $w = w_2(\theta)$.

Proof. The conditions (i) and (ii) are shown similarly to Proposition 1. We consider the third condition. Note that $\dot{u}_i(\theta)$ and $\dot{v}_i(\theta)$ ($i = 1, 2$) are the real and the imaginary parts of $\frac{dw_i}{d\theta}$. In terms of the conformal mapping $g(\zeta)$, it is explicitly given by

$$(11) \quad \frac{dw_i}{d\theta} = \frac{dg(\zeta)}{d\zeta} \frac{d\zeta}{d\theta} \Big|_{\zeta=g^{-1}(w_i(\theta))} = \begin{cases} g'(e^{i\theta})(ie^{i\theta}), & i = 1, \\ g'(\rho e^{i\theta})(i\rho e^{i\theta}), & i = 2. \end{cases}$$

Hence, in the quotient space $\mathbb{R}/\pi\mathbb{Z}$, we have

$$(12) \quad \nu_i(\theta) = \arg \frac{dw_i}{d\theta} = \arg g'(g^{-1}(w_i(\theta))) + \left(\theta - \frac{\pi}{2} \right).$$

Because of Proposition 1, evaluating the real parts of the first term and the second term of (10) at the boundary $w = w_i(\theta)$, we obtain $\theta - \frac{\pi}{2}$ and $\arg g'(g^{-1}(w_i(\theta)))$,

which agrees with the boundary value (12). Hence, the boundary condition (iii) is satisfied. $\square$

Using Proposition 2, we compute the cell alignments on some doubly connected domains inside the unit circle $\mathbb{D}$. Let Ω_1 and Ω_2 denote domains in the complex w -plane whose boundaries are parameterized by

$$(13) \quad \partial\Omega_1 = 0.5e^{i\pi/6}(\cos\theta + 0.6i\sin\theta) - 0.1 - 0.1i,$$

$$(14) \quad \partial\Omega_2 = 0.4(1 + 0.3\cos 3\theta)e^{i\theta},$$

for $\theta \in [0, 2\pi)$. Figure 5 shows the cell alignments on the doubly connected domains $\mathcal{D}_1 := \mathbb{D} \setminus \Omega_1$ and $\mathcal{D}_2 := \mathbb{D} \setminus \Omega_2$, in which we confirm that the angle of the cell alignments tangent to both boundaries. Note that the conformal mapping $g(\zeta)$ is numerically constructed using `conformal2` of Chebfun [25].

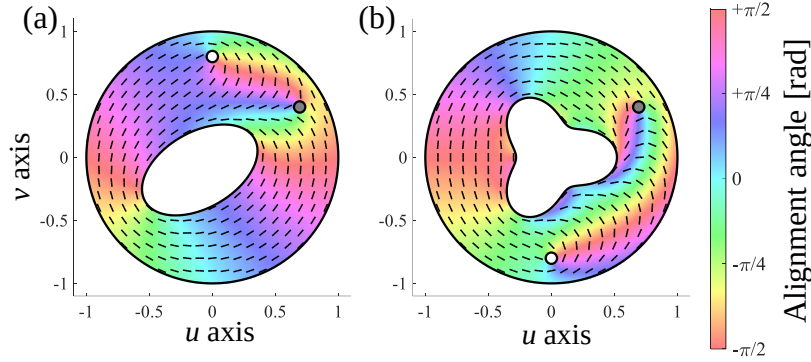


FIGURE 5. Cell alignments on the doubly connected domains computed with the analytic formula (10). The white and the gray circles represent the defects with the topological charges $q_1 = +1/2$ and $q_2 = -1/2$ respectively. (a) The domain is $\mathcal{D}_1 = \mathbb{D} \setminus \Omega_1$. The locations of the defects are $w_1 = 0.8e^{+i\pi/2}$ and $w_2 = 0.8e^{+i\pi/6}$ with $Q_n = Q_0$. (b) The domain is $\mathcal{D}_2 = \mathbb{D} \setminus \Omega_2$. The locations of the defects are $w_1 = 0.8e^{-i\pi/2}$ and $w_2 = 0.8e^{+i\pi/6}$ with $Q_n = Q_0$.

3.3. Detection of stable defects minimizing elastic energy. Since the defect locations are nothing but free parameters in the analytic formulae, we need to determine them from physical points of view. As discussed in [1], they are physically characterized as the minimizer of the Frank elastic energy F for the cell populations. According to (1), the Frank elastic energy in the domain D_w is specified by

$$(15) \quad F = \frac{K}{2} \iint_{\tilde{\mathcal{D}}_w} |\nabla \phi_{\mathcal{D}_w}|^2 dudv,$$

where $\tilde{\mathcal{D}}_w = \mathcal{D}_w \setminus \bigcup_{k=1}^N D_k$ is the domain removing disks $D_k(\epsilon) = \{w_k + re^{i\theta} \mid 0 < r \leq \epsilon, 0 \leq \theta < 2\pi\}$ of small radius ϵ . Since the elastic energy is a function of the defect locations $\mathcal{W}$ (or $\mathcal{Z}^*$), the defect locations are determined so that the elastic energy becomes the minimum. For the sake of simplicity, we assume $K/2 = 1$ in what follows. On the use of Green's theorem and the analytic formula (10) with

the conformal mapping $w = g(\zeta)$, the elastic energy is rewritten in the form of the boundary integral.

$$(16) F_n(\mathcal{Z}^*) = \frac{1}{2i} \oint_{\partial\tilde{\mathcal{D}}} \left(\frac{\partial f_{\mathcal{D}}(\zeta; \mathcal{Z}^*)}{\partial \zeta} - i \frac{g''(\zeta)}{g'(\zeta)} \right) \overline{(f_{\mathcal{D}}(\zeta; \mathcal{Z}^*) - i \log g'(\zeta))} d\zeta,$$

where $\tilde{\mathcal{D}} = g^{-1}(\tilde{D}_w)$ and

$$(17) \quad \frac{\partial f_{\mathcal{D}}(\zeta; \mathcal{Z}^*)}{\partial \zeta} = - \sum_{k=1}^N i q_k [R(\zeta, z_k) + R(\zeta, 1/\bar{z}_k)] - \left(i + \frac{Q_n}{\log \rho} \right) \frac{1}{\zeta},$$

$$(18) \quad R(\zeta, \alpha) = \frac{1}{\zeta - \alpha} + \sum_{\ell=1}^{\infty} \left(\frac{1}{\zeta - \rho^{-2\ell}\alpha} + \frac{\rho^{2\ell}\alpha}{\zeta(\zeta - \rho^{2\ell}\alpha)} \right).$$

Owing to $Q_n = n\pi + \sum_{k=1}^N q_k(\theta_k + \pi)$ for a fixed $n \in \mathbb{Z}$, the elastic energy F_n depends on n .

Since F_n becomes the function of the defect location $z_k \in \mathcal{Z}^*$ and $\bar{z}_k$, $k = 1, 2, \dots, N$, we compute local minimum by considering the gradient of F_n with respect to these variables. The gradient of the boundary integral F_n with respect to $\bar{z}_k$ is given by

$$(19) \quad \frac{\partial F_n}{\partial \bar{z}_k} = -\frac{1}{2i} \oint_{\partial\tilde{\mathcal{D}}} \left(\frac{\partial^2 f_{\mathcal{D}}(\zeta; \mathcal{Z}^*)}{\partial \bar{z}_k \partial \zeta} \overline{(f_{\mathcal{D}}(\zeta; \mathcal{Z}^*) - i \log g'(\zeta))} + \left(\frac{\partial f_{\mathcal{D}}(\zeta; \mathcal{Z}^*)}{\partial \zeta} - i \frac{g''(\zeta)}{g'(\zeta)} \right) \overline{\left(\frac{\partial f_{\mathcal{D}}(\zeta; \mathcal{Z}^*)}{\partial \bar{z}_k} \right)} \right) d\zeta,$$

in which

$$(20) \quad \frac{\partial^2 f_{\mathcal{D}}}{\partial \bar{z}_k \partial \zeta} = -\frac{1}{(1 - \bar{z}_k \zeta)^2} - \sum_{\ell=1}^{\infty} \left(\frac{\rho^{2\ell}}{(1 - \rho^{2\ell} \bar{z}_k \zeta)^2} + \frac{\rho^{2\ell}}{(\bar{z}_k \zeta - \rho^{2\ell})^2} \right) - \frac{i q_k}{2 \bar{z}_k \log \rho} \frac{1}{\zeta},$$

$$(21) \quad \frac{\partial f_{\mathcal{D}}}{\partial z_k} = \frac{1}{z_k - \zeta} + \sum_{\ell=1}^{\infty} \left(\frac{\rho^{2\ell} \zeta}{z_k(z_k - \rho^{2\ell} \zeta)} + \frac{\rho^{2\ell}}{\rho^{2\ell} z_k - \zeta} \right) + \frac{i q_k}{2 z_k \log \rho} \log \zeta.$$

We find the energy-minimizing configuration using the steepest descent,

$$(22) \quad z_k \rightarrow z_k - \alpha \frac{\partial F_n}{\partial \bar{z}_k},$$

in which $\alpha > 0$ is a parameter and it will be specified later. Let us note that the energy-minimizing configuration obtained here provides a local energy minimizer since n is a fixed parameter. In other words, it is equivalent to choose the branch of the logarithmic function where the topological defects exist. Hence, to be the global energy-minimizer, we need to consider $\min_n F_n$ among infinitely many local energy-minimizers.

The energy-minimizing procedure continues until the defects hardly move or some defects collide, called annihilation, up to a numerical tolerance. When the procedure terminates by annihilation, it does not necessarily provide an energy minimizer. In this case, by merging these collided defects into one defect, we need to continue the energy-minimizing procedure with less number of defects although we do not proceed to this step in this paper.

4. BOUNDARY SYMMETRY AND ENERGY MINIMIZING DEFECTS OF CELL ALIGNMENTS

4.1. Numerical methods. The integration path of the line integrals (16) and (19) is defined as shown in Figure 6. The branch cut γ_0 of the function $\log \zeta$ is chosen as the negative real axis. For $k = 1, \dots, N$, the branch cut γ_k of the function $\log \omega(\zeta, z_k)$ in the first term of $f_{\mathcal{D}}$ is taken by

$$(23) \quad \gamma_k = \begin{cases} \{re^{i\theta_k} \mid |z_k| < r\} & (q_k > 0), \\ \{re^{i\theta_k} \mid 0 < r < |z_k|\} & (q_k < 0). \end{cases}$$

The integral path along the branch cut γ_k is defined as $\Gamma_k := \gamma_k \cap \tilde{\mathcal{D}}$. We now suppose that there are d defects with the charge $+1/2$ and d defects with the charge $-1/2$, namely $N = 2d$, whose locations are denoted by $z_1, \dots, z_d$ and $z_{d+1}, \dots, z_{2d}$ respectively. We subscript $z_1, \dots, z_d$ and $z_{d+1}, \dots, z_{2d}$ in ascending and descending orders of their arguments, respectively. By c_k , we express the intersecting point of Γ_k and the boundaries of the annular domain $\mathcal{D}$. Owing to the definition of Γ_k , the point c_k is located at the outer boundary for the positive defects, while it is at the inner boundary for the negative defects. The shorter arc of the unit circle going in the counter-clockwise direction from c_k to c_{k+1} is referred to as C_k for $k = 1, \dots, d-1$. The counter-clockwise path C_0 is the arc of the unit circle from $z = e^{-i\pi}$ to c_1 , and C_d also denotes the counter-clockwise arc of the unit circle from c_d to $z = e^{i\pi}$. Similarly, we can define the clockwise arcs $-C_k$ along the inner boundary $|\zeta| = \rho$ for $k = d+1, \dots, 2d$. With these notations, we can set the integration path as follows. We start from $z = e^{-i\pi}$, track C_0 , and go along $-\Gamma_k, g^{-1}(-\partial D_k), \Gamma_k$ and C_k for $k = 1, \dots, d$, and reach $e^{i\pi}$. Here, $-\Gamma_k$ denotes the path in the opposite direction of Γ_k . The integration path continues to the inner boundary through $-\Gamma_0$ and goes in the clockwise direction from $z = \rho e^{i\pi}$ to $z = \rho e^{-i\pi}$ by passing $-C_k, \Gamma_k, g^{-1}(-\partial D_k)$ and $-\Gamma_k, k = d+1, \dots, 2d$ in order and $-C_{2d+1}$. Then it finally returns to the original position $e^{-i\pi}$ through Γ_0 .

When we compute $\log \omega(\zeta, z_k)$ and $\log \omega(\zeta, 1/\bar{z}_k)$, we use the following formula so that the branch cut of the numerical computation agrees with Γ_k as defined.

$$\begin{aligned} \log \omega(\zeta, z_k) &= \begin{cases} \log(-z_k) + \log(1 - \zeta/z_k) + \sum_{\ell=1}^{\infty} [\log(1 - \rho^{2\ell}\zeta/z_k) + \log(1 - \rho^{2\ell}z_k/\zeta)] & (q_k > 0), \\ \log \zeta + \log(1 - z_k/\zeta) + \sum_{\ell=1}^{\infty} [\log(1 - \rho^{2\ell}\zeta/z_k) + \log(1 - \rho^{2\ell}z_k/\zeta)] & (q_k < 0). \end{cases} \\ \log \omega(\zeta, 1/\bar{z}_k) &= \log(-1/\bar{z}_k) + \log(1 - \bar{z}_k\zeta) + \sum_{\ell=1}^{\infty} [\log(1 - \rho^{2\ell}\bar{z}_k\zeta) + \log(1 - \rho^{2\ell}/(\bar{z}_k\zeta))]. \end{aligned}$$

The infinite summation can be truncated by $\ell = 10$ terms owing to the rapid convergence. The conformal mapping $g(\zeta)$ is numerically constructed using `conformal2` of Chebfun [25]. On the use of Cauchy's theorem, we use the series expansion to compute the derivative of the conformal mapping.

$$\begin{aligned} g(\zeta) &= \frac{1}{2\pi i} \oint_{|z|=1} \frac{g(z)}{z - \zeta} dz - \frac{1}{2\pi i} \oint_{|z|=\rho} \frac{g(z)}{z - \zeta} dz \\ &= \sum_{m=0}^{\infty} \zeta^m \left(\frac{1}{2\pi} \int_0^{2\pi} g(e^{i\theta}) e^{-im\theta} d\theta \right) + \sum_{m=1}^{\infty} \left(\frac{\rho}{\zeta} \right)^m \left(\frac{1}{2\pi} \int_0^{2\pi} g(\rho e^{i\theta}) e^{im\theta} d\theta \right). \end{aligned}$$

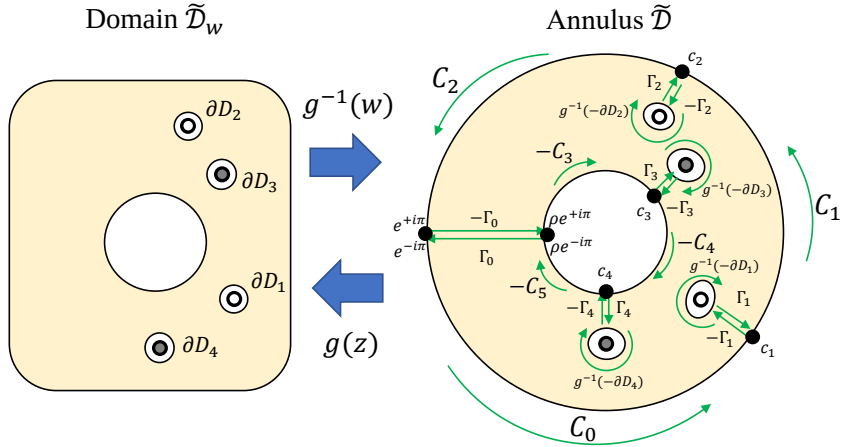


FIGURE 6. The integration path for the line integrals (16) and (19) for the four defects, i.e. $d = 2$. The white and the gray circles represent the defects with the topological positive and negative charges respectively.

In actual numerical computations, the series expansion is truncated by $m = 1000$ and the coefficient of ζ^m is obtained by the Fourier series coefficients of the boundary value of the function $g(\zeta)$. The derivative of $g(\zeta)$ is computed by differentiating the series. We utilize the fast procedure `aaa` in Chebfun to construct these functions numerically. For the path integrals (16) and (19), we fix the radius of the small disk $D_k(\epsilon)$ and the step size of the energy minimizing process (22) to $\epsilon = 0.01$ and $\alpha = 0.001$. We stop the minimizing procedure when the distance between two defects is less than 4ϵ since it means the two defects are close enough to be annihilated.

4.2. Numerical results.

4.2.1. *Concentric annuli.* Before solving the minimization problem, we first fix two defects on the real axis, i.e. $z_1 = r_1$, $z_2 = r_2$, with the topological charges $q_1 = -1/2$ and $q_2 = +1/2$ on the concentric annulus $\mathcal{D}$ as shown in Figure 7(a), and we then compute the elastic energy for (r_1, r_2) with $\rho < r_1 < r_2 < 1$. Note that the free parameter Q_0 in $f_{\mathcal{D}}$ vanishes since the arguments of the two defects are the same in this case. When the two defects are separated, the cell alignment like Figure 7(b) is observed, while the direction of the cell alignment completely goes along the annulus for the defects at the same location as shown in Figure 7(c). Figure 7(d,e,f) are the contour plots of the elastic energy for (r_1, r_2) for the radii $\rho = 0.05, 0.1$ and 0.2 of the annulus $\mathcal{D}$ respectively. For each case, the elastic energy gets smaller along the diagonal line $r_1 \approx r_2$, which corresponds to the annihilation of the two defects. This indicates that the energy without defects is more stable than that with the two close defects. For $\rho = 0.05$, we observe a local minimum in the neighborhood of $r_1 = \rho$ in Figure 7(d), indicating the existence of an energy-minimizing configuration of the two distinct defects. For $\rho = 0.1$, the local minimum becomes observed more clearly in Figure 7(e), but it disappears for $\rho = 0.2$ in Figure 7(f).

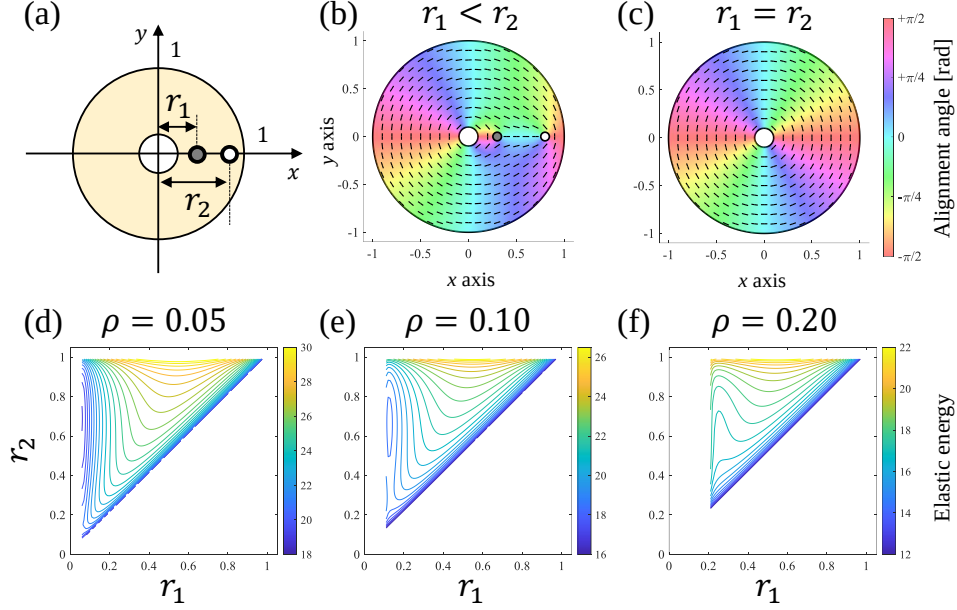


FIGURE 7. The elastic energy with the two defects on the real axis in the annulus $\mathcal{D}$. (a) The configuration of the two defects. (b) A cell alignment for the two defects separated. (c) A cell alignment for the two defects at the same location (the case of annihilation). (d,e,f) The elastic energy for the two defects that are located at (r_1, r_2) on the real axis of the annulus with the radius (d) $\rho = 0.05$, (e) $\rho = 0.1$, (f) $\rho = 0.2$.

We solve the minimization problem of the elastic energy. Since the existing studies [17, 18] considered the topological defects on the boundaries, the initial guess of the topological defects with the positive charge $+1/2$ and the negative charge $-1/2$ for the energy-minimizing procedure (22) is set on the real axis, $z_1 = \rho + 2\varepsilon$ and $z_2 = 1 - 2\varepsilon$ for a small $\varepsilon > 0$ respectively. Figure 8(a) shows the defect trajectories for 1000 iterations of the energy-minimizing procedure when the radius of the annulus $\mathcal{D}$ is $\rho = 0.05, 0.1$, and 0.2 . The defects are moving along the real axis through the energy-minimizing steps. The change of the elastic energy corresponding to the iterations is shown in Figure 8(b). For each case, the energy decreases and converges to a certain constant. For $\rho = 0.2$, the two defects get closer and the procedure terminates by annihilation after 700 iterations. On the other hand, for $\rho = 0.05$ and 0.1 , the locations of the two defects are well separated and converged. This indicates the existence of energy-minimizing defects as expected in Figure 7(d,e). Figure 8(c) is the plot of the locations of the defects for various radius ρ of the annulus $\mathcal{D}$. As ρ tends to zero, the distance between the two defects increases. The topological defect with the charge $+1/2$ monotonically approaches the outer boundary, while the defect with the charge $-1/2$ moves towards the inner boundary though it does not touch the boundary. To discuss the continuity between the energy-minimizing configurations in the concentric annulus and the

simply connected disc, using the procedure [1], we compute the energy-minimizing defect in the simply connected disc when a topological defect with the charge $+1/2$ is fixed at the origin as shown in Figure 8(d). This situation is realized by collapsing the inner boundary, which formally converges the topological defect with the charge $+1$ as $\rho \rightarrow 0$, and the topological defect with the charge $-1/2$ at the origin. The location is found to be $z_s = 0.7071$, which is plotted in Figure 8(c) for reference. Since the location of the outer positive defect tends to be a constant z_s , this indicates that the energy-minimizing configuration of the topological defects in the concentric annulus connects continuously to that in the simply connected disc. On the other hand, the distance between the two energy-minimizing defects with the charges $\pm 1/2$ gets closer as ρ increases, but the energy-minimizing procedure terminates by annihilation for $\rho \geq 0.16$.

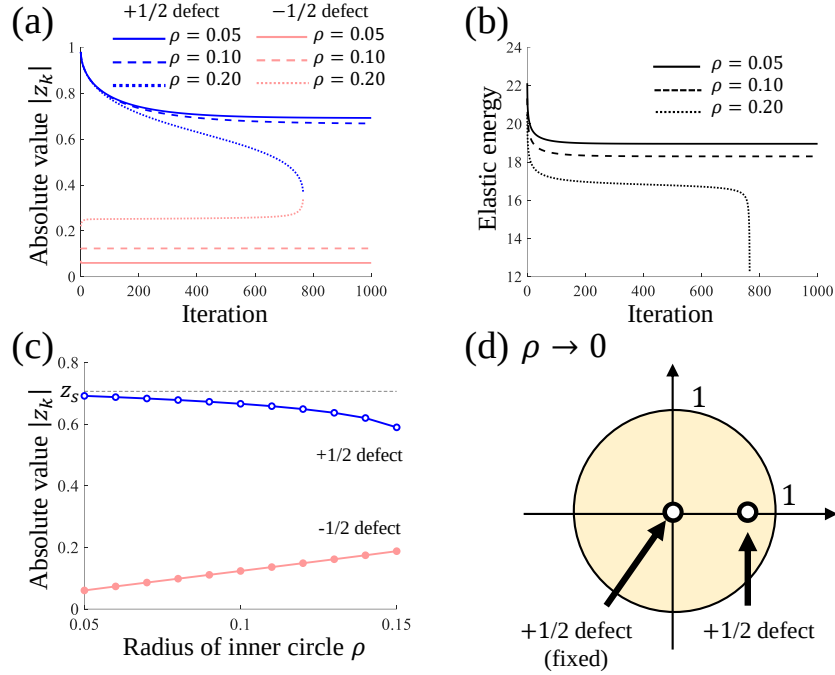


FIGURE 8. The energy-minimizing procedure for finding two defects with the topological charges $\pm 1/2$ moving along the real axes. (a) The trajectories of the locations of the two defects for the various radii $\rho = 0.05, 0.1$, and 0.2 . (b) The convergence of the elastic energy associated with the configurations for the radii $\rho = 0.05, 0.1$, and 0.2 . (c) The configurations of the energy-minimizing defects versus the radius ρ of the annulus. The dashed line $z_s = 0.7071$ represents the location of the topological defect with the charge $+1/2$ in the simply connected disc having a fixed topological defect with the charge $+1/2$ at the origin. (d) The configuration of the two defects in the disc, which corresponds formally to the case of the annulus as $\rho \rightarrow 0$.

We also investigate the dependence of initial defect positions on the final state of the defect pair for $\rho = 0.1$ as shown in Figure 9. In this simulation, we change the initial positions of the defects and check whether the defect pair is separated or annihilated after 5000 iterations of the energy-minimizing procedure. As a result, the defect pair is always annihilated when the initial position of the $-1/2$ defect is 0.5 or greater. In addition, the defect pair is separated when the distance between them is more than about 0.2 to 0.3. This result indicates the existence of the minimal distance of the defect separation, which can be predicted by the energy-minimizing procedure.

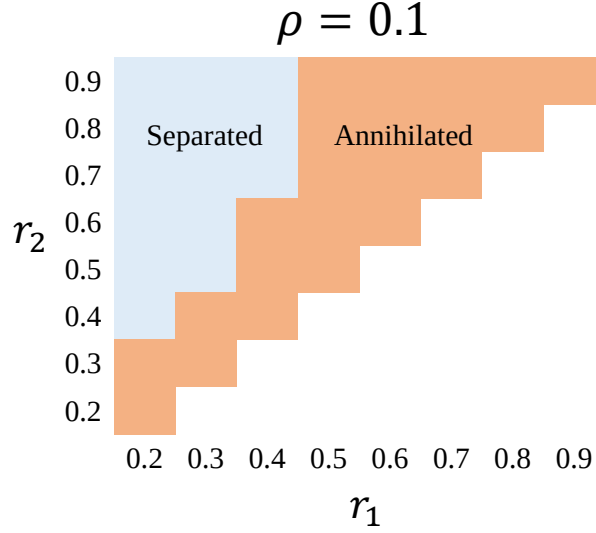


FIGURE 9. The dependence of initial defect positions on the final state of the defect pair. The horizontal and vertical axes express the initial positions of $-1/2$ and $+1/2$ defects, respectively. The blue and red color maps indicate the defect pair were separated or annihilated for each initial condition.

Suppose that we choose a different initial guess of the two defects with the topological charges $\pm 1/2$, which is symmetric about the real axis as in Figure 10(a). Then the trajectories of the two defects converge towards the energy-minimizing state, in which the two defects have the same argument, but the negative one is located near the inner boundary and the positive one is near the outer boundary. Figure 10(b) shows the energy-minimizing configuration of the pairs of two defects $d = 2$ (i.e. $N = 2d = 4$), where two defect pairs rotate repulsively and they converge on opposite locations. We show other configurations of multiple defect pairs starting from $N = 2d = 6$ and $N = 2d = 8$ in Figure 10(c) and (d), respectively. Although they moved so that they had a rotational symmetry of $2\pi/3$ ($d = 3$) or $\pi/2$ ($d = 4$), some defect pairs annihilate in the final state, which means they are not energy-minimizing configurations.

It is noted that the energy-minimizing state varies according to the radius of the small disk $D_k(\epsilon)$ because the elastic energy F_n is a function of ϵ as well as

the defect positions. As $\epsilon \rightarrow 0$, the energy itself diverges to infinity, but there are some cases where the minimum point of energy converges to a certain value. For simply connected domains, these cases have been obtained analytically in the existing studies [21, 1]. The extension of the analytic method to annuli is not straightforward, which would be a future work.

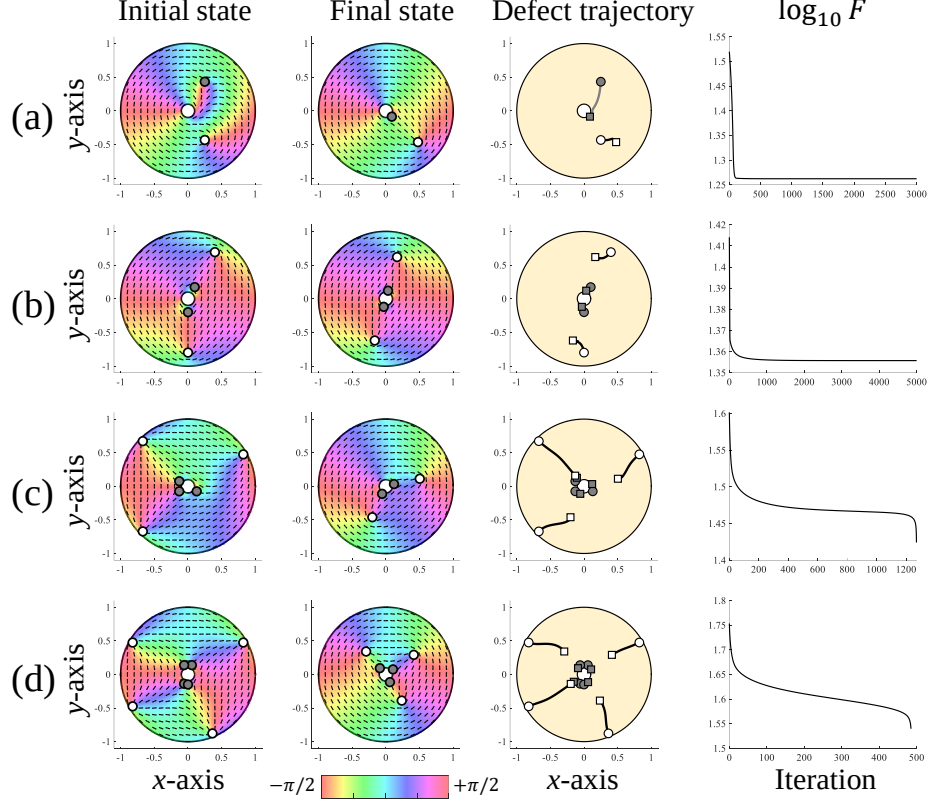


FIGURE 10. The energy-minimizing configurations of defect pairs. (a) One pair of two defects. ($d = 1, N = 2d = 2$) (b) Two pairs of two defects. ($d = 2, N = 2d = 4$) (c) Three pairs of two defects. ($d = 3, N = 2d = 6$) (d) Four pairs of two defects. ($d = 4, N = 2d = 8$) The radius of the inner boundary of $\mathcal{D}$ is $\rho = 0.1$. In the initial and final state columns, the white and the gray circles represent the defects with the topological charges $\pm 1/2$ respectively. In the defect trajectory column, the white and the gray circles/squares represent the initial/final positions of the defects with the topological charges $\pm 1/2$ respectively.

4.2.2. Anisotropic domains with corners. Owing to the rotational symmetry of the concentric annulus $\mathcal{D}$, the energy-minimizing process cannot control the argument of the defect configurations nor the annihilation. We thus break the symmetry of

the domain to fix them by considering an anisotropic domain with rounded corners. To this end, we consider the following three cases.

Case A: The outer boundary of the domain has four rounded corners and the inner boundary is a circle with radius $\rho = 0.1$. The outer boundary $\partial\Omega_A$ is represented by

$$\partial\Omega_A := \{z = x + iy \in \mathbb{C} \mid x^6 + y^6 = 0.5\}.$$

Case B: The outer boundary is the unit circle. The inner boundary has four rounded corners and it is represented by

$$\partial\Omega_B := \{0.1z \mid z \in \partial\Omega_A\}.$$

Case C: Both outer and inner boundaries have four rounded corners, which are represented by $\partial\Omega_A$ and $\partial\Omega_B$, respectively. To further break the symmetry of the domain, we also consider the angular rotations by $\pi/8$ and $\pi/4$ for the inner boundary.

In all cases, the conformal mapping $g(\zeta)$ is numerically constructed using `conformal2` of Chebfun [25].

When the outer boundary of the domain has four corners (Case A), the energy-minimizing state consists of the defect with the charge $+1/2$ around the corner of the outer boundary and the defect with the charge $-1/2$ near the inner boundary with the same argument (Figure 11(a)). The energy-minimizing state is always the same for different choices of initial configurations as shown in the right panels of Figure 11(a). On the other hand, for the inner boundary with the four corners (Case B), we find two different energy-minimizing configurations depending on the initial choice, where the two defects are aligned along the line on the same argument $\pi/4 \pm \delta$ for a small $\delta > 0$ near the corner (Figure 11(b)).

The energy-minimizing trajectory of a positive defect for Case A is shown in Figure 12(a), which indicates that the defect first moves along the imaginary axis, changes its direction, and finally converges to the final state around the outer corner. This behavior indicates the existence of a saddle point of the elastic energy around which the trajectory of the defects changes. This is verified by computing the gradient of the energy $|\partial F/\partial z_1|$ and $|\partial F/\partial z_2|$ when the two defects are aligned along the line of arguments $\pi/2$ and $\pi/4$ as shown in Figure 12(b). The contour plot of the gradients for the argument $\pi/2$ in Figure 12(c) shows that the configuration of the two defects symbolized as triangles in Figure 12(b) is a critical point of the energy gradient. The diagonalized Hesse matrix around the critical point is $H_1 = \text{diag}[-0.0031, 0.0044, 0.2612, 1.6860] \times 10^3$, which means the critical point is a saddle point. On the other hand, according to the contour of the gradients in Figure 12(d) for the argument $\pi/4$, the configuration of the two defects symbolized by squares is also a critical point. Its corresponding diagonalized Hesse matrix is given by $H_2 = \text{diag}[0.0386, 0.1770, 1.1450, 2.0871] \times 10^3$. Hence, the critical point is a local minimum.

We increase the number of defects and consider the energy-minimizing configurations in the domain bounded by the rounded square. Figure 13(a, b) shows the initial states of two defect pairs ($d = 2, N = 4$) and the final states after the energy-minimizing procedure. We observe that the positive defects are moving toward one of the four rounded corners and the negative defects are aligned along the same arguments as the positive ones. The chosen corners in the final state depend on the initial state. Because the rotational symmetry of the domain is broken due to

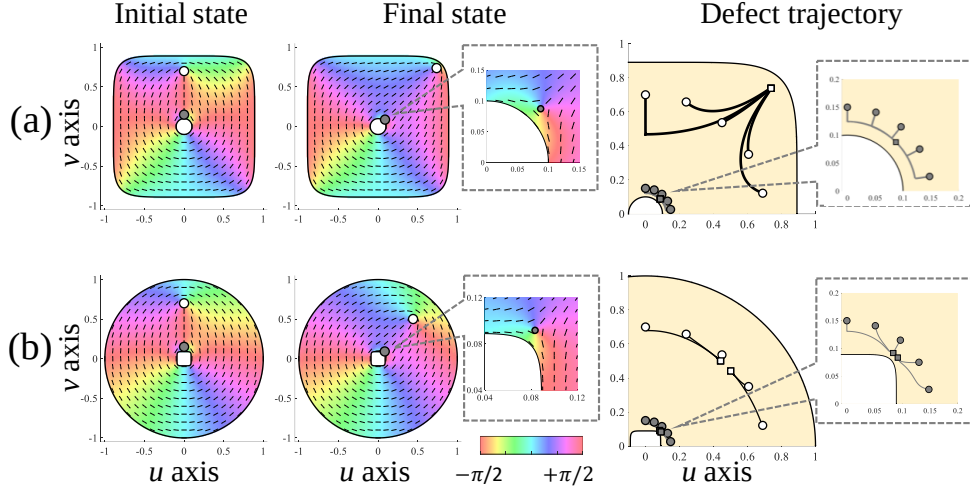


FIGURE 11. The convergence to the energy-minimizing procedure after 5000 iterations. (a) The case when the outer boundary of the domain has four rounded corners (Case A). (b) The case when the inner boundary of the domain has four rounded corners (Case B). The initial state of the two defects with $+1/2$ and $-1/2$ are given by $0.7e^{i(\pi/2-m\pi/9)}$ and $0.15e^{i(\pi/2-m\pi/9)}$, $m = 0, 1, \dots, 4$. In the initial and final state columns, the white and the gray circles represent the defects with the topological charges $\pm 1/2$ respectively. In the defect trajectory column, the white and the gray circles/squares represent the initial/final positions of the defects with the topological charges $\pm 1/2$ respectively.

corners, the final states are restricted along the diagonal lines. This behavior is also observed for three ($d = 3, N = 6$) and four ($d = 4, N = 8$) defect pairs as shown in Figure 13(c, d). Considering that the three or four defect pairs annihilate for the concentric annulus as in Figure 10(c, d), the corner effects of the outer boundary play an important role in suppressing the annihilation of the defect pairs as well as controlling the defect positions. Hence, the existence of boundary corners could control the energy-minimizing configuration of the defects. It is also noted that the initial states of the defect pairs are also important for determining whether the defect pairs annihilate or not. For three defect pairs ($N = 6$) in Figure 13(e), the two pairs are aligned along the diagonal lines, where the other pair annihilates in the middle. As a result of the annihilation, we obtain the energy-minimizing configuration of $N = 4$ defects as we obtain in Figure 13(a).

We finally consider the energy-minimizing configurations of two defects in domains whose outer and inner boundaries are both rounded squares (Case C). Although the outer boundary with four rounded corners is the same as that in Figure 12, the inner rounded square boundary is rotated around the origin by the angles 0 in Figure 14(a), $\pi/8$ in Figure 14(b) and $\pi/4$ in Figure 14(c). For the domain in Figure 14(a), wherever the initial states are chosen, the defects $+1/2$ and $-1/2$ move toward the corners of the outer and inner boundaries, and the energy-minimizing

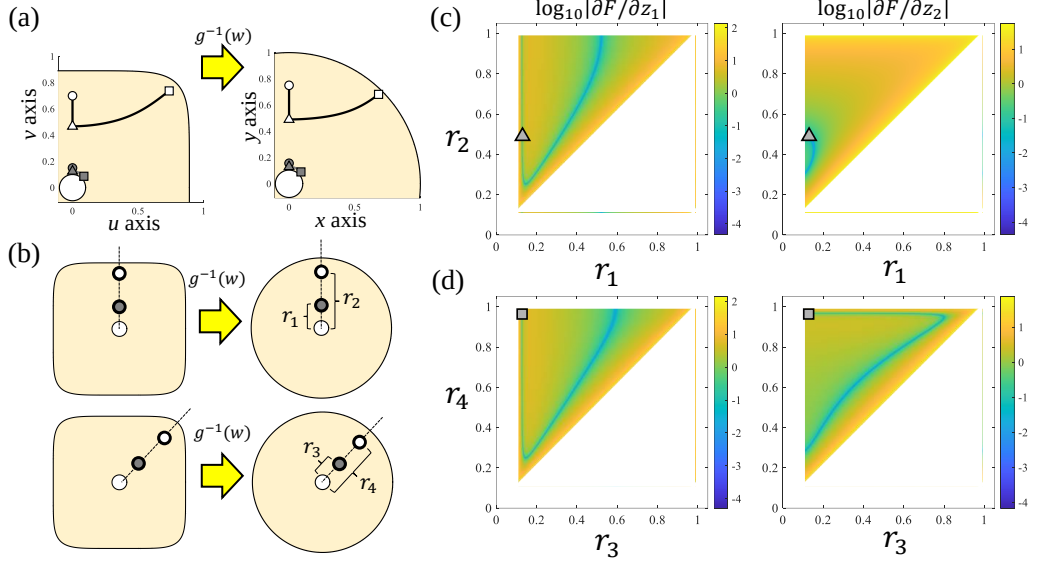


FIGURE 12. The gradient of the elastic energy. (a) The configuration of the two defects. The defect with the charge $-1/2$ is located at $r_1 e^{i\pi/2}$ and $r_3 e^{i\pi/4}$. The location of the defect with the charge $+1/2$ is given by $r_2 e^{i\pi/2}$ and $r_4 e^{i\pi/4}$. (b) The energy-minimizing trajectories of the defects. (c) The components of the energy gradient for the defects aligned along the argument $\pi/2$. (d) The components of the energy gradient for the defects aligned along the argument $\pi/4$. In the initial and final state columns, the white and the gray circles represent the defects with the topological charges $\pm 1/2$ respectively. In the defect trajectory column, the white and the gray circles/squares represent the initial/final positions of the defects with the topological charges $\pm 1/2$ respectively.

state is given by the pattern (a-1). On the other hand, for the domains with misaligned boundaries in Figure 14(b), we find two energy-minimizing configurations (b-1) and (b-2) depending on the initial states. Figure 10(c) also yields two energy-minimizing configurations (c-1) and (c-2), but they are different from those for the other cases. In (c-1), the two defects with charges $\pm 1/2$ move toward the corners of the outer and inner boundaries. However, in (c-2), the negative defect is located around the corner of the inner boundary, while the positive one stays in the middle. This type of energy-minimizing state is allowed since the domain of Figure 14(c) has more symmetry than the domain in Figure 14(b). Hence, the intrinsic symmetry of the domain determines the variety of energy-minimizing configurations.

According to our simulations, the defects tended to be located around rounded corners after the energy-minimizing procedure. The existing studies [14, 24] also showed the defects preferred to be located around sharp corners, which is consistent with the present simulations. To further investigate the effects of sharp corners on the defect positions, it would be suitable to use Schwartz-Christoffel maps in

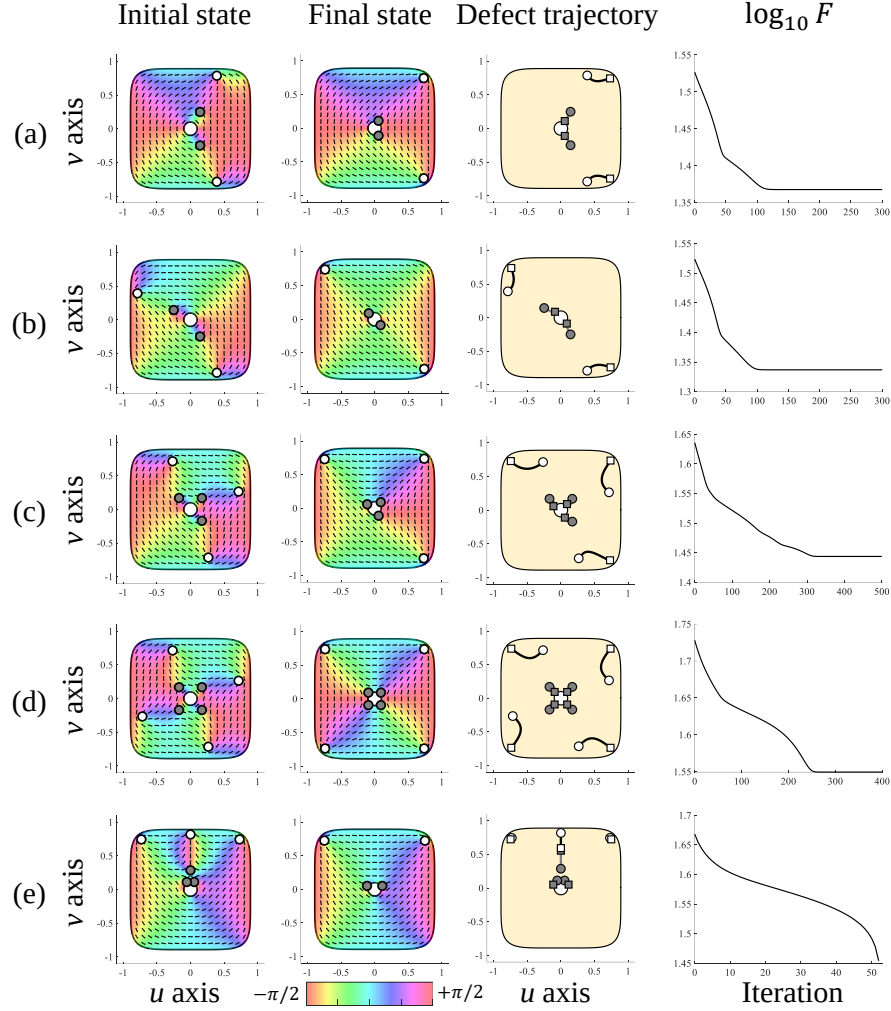


FIGURE 13. The energy-minimizing procedure for several pairs of defects in the domain bounded by the rounded square. (a) $N = 4$. (b) $N = 4$. (c) $N = 6$. (d) $N = 8$. (e) $N = 6$.

the same way as the existing studies [14, 24]. However, it is practically difficult to compute the energy numerically due to the existence of singularities on the integration path coming from the conformal map. To resolve this numerical issue, we need to choose an appropriate integration path avoiding the singularities, which will be investigated in future studies.

Our numerical results indicate that the positions of the defect pairs can be controlled by making corners on inner or outer boundaries. However, the number of the energy-minimizing state increases when the corners on the boundaries are misaligned in Figure 14(b,c). Since the final position of the defect pairs depends on the initial cell alignment and it is difficult to control the initial alignment in cell culturing experiments, it would be better to suppress the variety of energy-minimizing

configurations from the viewpoint of the reproducibility of the experiments. Thus, the aligned corners in Figure 14(a) would be a better geometry compared to the others in Figure 14(b,c). For decreasing the energy-minimizing configurations, we can consider further breaking of the symmetry because the geometries in Figure 11 and 14 still have the four-fold rotational symmetry. Our future work would include the optimization of the geometry which has fewer energy-minimizing states to achieve reproducible generation of the defect pairs.

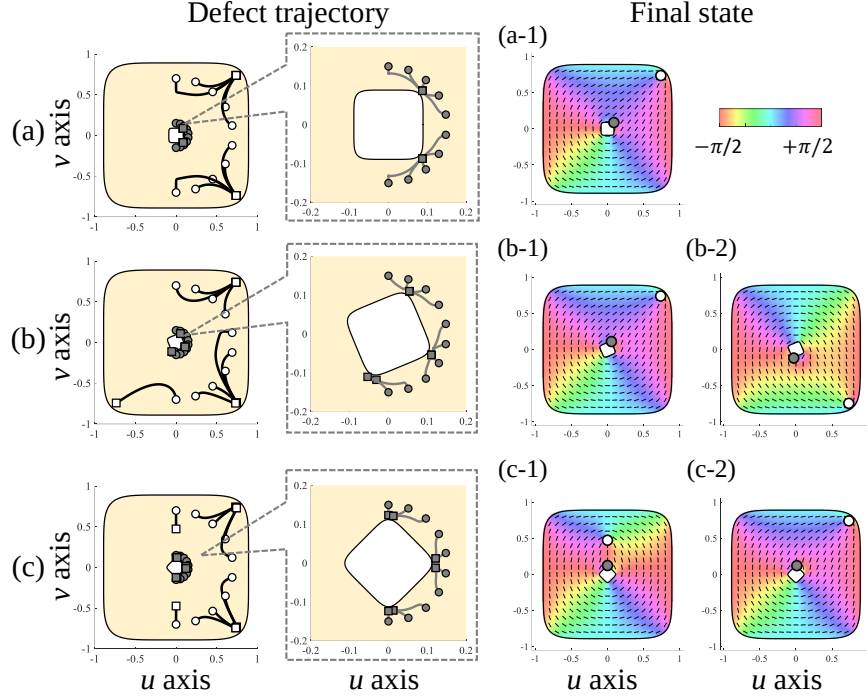


FIGURE 14. The energy-minimizing configurations of the two defects in the domain bounded by the inner and the outer rounded squares (Case C). The inner square is rotated by the angle (a) 0, (b) $\pi/8$, (c) $\pi/4$. In this energy-minimizing procedure, the initial locations of the defects with charges $\pm 1/2$ are given $0.7e^{i(\pi/2-m\pi/9)}$ and $0.15e^{i(\pi/2-m\pi/9)}$, $m = 0, 1, \dots, 9$ respectively. In the defect trajectory column, the white and the gray circles/squares represent the initial/final positions of the defects with the topological charges $\pm 1/2$ respectively. In the final state column, the white and the gray circles represent the defects with the topological charges $\pm 1/2$ respectively.

5. CONCLUSION

Based on the model of nematic liquid crystals, we derived an analytical formula describing the orientation of cells in biological tissues in doubly connected annuli. This solution formula allows the existence of a finite number of topological defects

in the domains whose orientation cannot be well-defined, and the configuration of these defects is obtained as a minimizer of Frank elastic energy of the nematic liquid crystal. This is an extension of the analytic formula in the simply connected domains by Miyazako and Nara[1]. With this formula and conformal mapping, we can observe the formation of orientational orders created by cell orientation in doubly connected domains with arbitrary smooth boundaries.

The configuration of the topological defects minimizing the elastic energy is numerically obtained by the steepest descent method. For concentric annuli, since the defects with opposite signs collide with each other, the energy minimum solution is not obtained in some cases. On the other hand, when an energy minimum is attained, the defect with the negative strength is located near the inner boundary, and that with the positive strength stays at the outer boundary. When the boundary is square-shaped and does not have the same rotational symmetry as a concentric annulus, the annihilation of the defects is less likely to occur, whereas the energy-minimizing defects are often located at the corners of the internal and outer square. This suggests that the position of the defect pair can be controlled to some extent by deforming the boundary shape in an appropriate manner.

It is noted that we treated the defects as point-like objects in this study to obtain the configuration of the topological defects minimizing the elastic energy; however, recent studies revealed that defects have finite size and polar structures and investigated the motion of defects by modeling the direction of the defects and considering the aligning torque [26, 27, 28]. Thus, in our study, the defect motion cannot be fully predicted by the defect trajectories during the energy optimization because we neglected the contributions of the defect directions and aligning torque. Since the existing study also adopted complex analysis formulation [27], we expect our proposed formulae will be extended to the prediction of defect motions by incorporating the contributions of the defect direction and aligning torque.

Finally, we discuss future directions: This solution formula includes a parameter Q_n that is prescribed in advance when the energy-minimizing procedure starts. As mentioned in this paper, choosing Q_n means fixing one special branch of the logarithmic function where the topological defects exist. We thus need to compare the numerical results with experimental studies of the orientational order of actual cells to see which Q_n is valid. It is also interesting to construct the conformal map from the concentric annulus to a given doubly connected domains with various boundaries to investigate the relation between the configuration of the defects and the boundary shapes. In addition, since the proposed formulae in this paper are expressed in terms of the SKP functions, they could be extended for solving many physical problems in domains with higher connectivity. In this case, the total sum of the topological charges becomes $M - 2 < 0$ for M -connected domain ($M \geq 3$), which means we should consider the detection of stable defects whose topological charges were negative. While it is easy to replace the SKP function of the first term in the equation (6) with SKP functions for higher connected domains provided in [23], we expect it would not be easy to adjust the boundary condition with the complementary terms corresponding to the second and third terms in the equation (6). Thus, it is necessary to consider other approaches to derive the formulae for higher connected domains. Moreover, it is of significance as a future topic to develop a numerical method for solving the inverse problem of finding the boundary shape that achieves the given defect configuration through this analytic formula.

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