Beyond displays: The recent progress of liquid crystals for bio/chemical detections

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Liquid crystals (LCs) are often known as electronic displays and have become ubiquitous in our daily life, apart from that, in the past 10 years, LCs have been investigated as exquisitely sensitive reporters for developing new molecular sensing and detection tools. The unique and primary advantage of this class of intriguing materials is the perturbation of the local ordering LCs at molecular scale by bio/chemical species can be communicated within LC molecules and extended over microns, allowing the observation of the optical signals by microscope or even the naked eye. Therefore, it provides a new platform for developing bio/chemical detection and potentially label-free sensing systems.

liquid crystals, detection, interfaces, amplification, transduction

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In March 1888, a young botanist called Friedrich Reinitzer [1] first found that esters of cholesterol appeared to have two melting points between which the liquid showed iridescent colors and birefringence. Actually he discovered a new phase of matter: a liquid crystalline phase, distinguished from solids, liquids and gases that are already familiar to us [2]. Substances in this fourth state are called liquid crystals (LCs), flowing like a conventional liquid and exhibiting orientational order like a crystalline solid. In general, the molecules forming LCs are anisotropic, either rod-like or disc-like. There are two basic classes of LCs: *thermotropic* and *lyotropic*. In the *thermotropic* system, the liquid crystalline phase only exists within a particular temperature range, between a melting point, T_m , and an upper transition temperature, T_c (Figure 1). In the *lyotropic* system, LCs possess polar and non-polar parts within the same molecule. In a certain concentration range, molecules organize themselves into ordered structures showing LC properties. This review will not discuss lyotropes further

Figure 1 Molecular structure of 5CB and different organizations of solid, liquid crystal and isotropic liquid phases.

and focus on thermotropic LCs, especially 4-cyano-4'-pentylbiphenyl (5CB), which exhibits liquid crystallinity in the nematic phase at room temperature, a simple and handy choice for constructing optical detectors performed at ambient condition.

The key principle of employing LCs for molecular detection is illustrated in Figure 2. The local interruption of LC ordering at the molecular scale can be amplified to micron

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Figure 2 Schematic illustration of the main principle of detection based on LCs.

scale, and transduces the anchoring transition into measurable optical output [3–7]. Owing to these fascinating properties, the LC-based analysis has great potential for developing rapid, simple and label-free detection. So far, three typical LC-based designs have been utilized: LC-solid interfaces, LC-aqueous interfaces and LC droplets. Accordingly, this review is divided into three sections, explains the main detection principles, summarizes most recent progress, followed by conclusions and perspectives.

1 LC-solid interfaces

The ordering of LCs is sensitive to the structure of surfaces, including nanoscale topography and the presence of self-assembled monolayers (SAMs), which have been well studied mostly driven by electronic display market [8]. Inspired by that, bio/chemically modified substrates have been explored to control LC ordering and designed for detecting biomolecules [9–14] or chemicals [15–20]. For example, as shown in Figure 3(a), the gold substrate was first treated with a mixture of biotin-(CH₂)₂[(CH₂)₂O]₂NHCO(CH₂)₁₁SH (BiSH) and CH₃(CH₂)₇SH (C₈SH). The two substrates were paired to form a LC cell with a thickness about 2 μm controlled by a spacer, and a drop of 5CB was drawn into the

Figure 3 (a) Schematic illustration of the binding of protein avidin to mixed SAMs containing biotin groups. Optical images with crossed polarizers of nematic 5CB sandwiched between mixed SAMs without (b) and with (c) bounded avidin. Reprinted with permission from [9]. Copyright 1998, Science.

cell through capillary force. As the gold was obliquely deposited onto glass substrate, the anisotropic roughness could induce 5CB to uniformly align on the plane (all LCs orient along the corrugation of the gold film). It was observed that though forming SAMs from BiSH and C₈SH, which did not erase the nanoscale topography and Figure 3(b) showed a dark and featureless image, indicating the 5CB within the cell remained the same orientation. However, the ordering of 5CB was interrupted due to the existence of avidin bounded onto the substrate (ca. 10¹⁰ avidin per mm²) (Figure 3(c)). This work demonstrates the possibility of using LCs to amplify and transduce the binding of proteins with ligands on solid substrates to optical signals.

Apart from decorating the solid substrates with ligands for detecting proteins, it is also feasible to modify the surface with chemical receptors for chemical detection [15–20]. Figure 4 showed that depending on the surface topology and chemical composition, 5CB aligned on the plane with orientation depicted in Figure 4(c). Due to the hydrogen bonding of 5CB with –COOH group immobilized on the surface (10–40 kJ/mol), 5CB underwent an orientation across the corrugation of gold film, combining the top surface decorated with methyl group (CH₃) directing an orientation of 5CB parallel to the topology, resulting in a twist LC cell, which appeared bright under the cross polarizers (Figure 4(a)). Upon exposure the acidic surface to a vapor of 12 ppmv hexylamine [*n*-H₂N(CH₂)₅CH₃] (HA), which led to acid-base interaction (>70 kJ/mol) and displaced 5CB, therefore, the LC cell turned to dark (Figure 4(b)), as no twisted LCs rotated polarized light (Figure 4(d)).

More interestingly, when the –COOH groups were pre-treated with transition metal ions, e.g. Cu²⁺, which coordinated with nitrile group of 5CB and caused 5CB aligning perpendicularly to the surface (homeotropic alignment), appeared dark under the polarized microscope. As the

Figure 4 Optical images with crossed polarizers of nematic 5CB sandwiched between mixed SAMs before (a) and after (b) exposure to HA. (c), (d) Schematic illustration of 5CB orientation in (a) and (b), respectively. Reprinted with permission from [15]. Copyright 2001, Science.

tailor the interfacial properties for versatile uses [50]. Note that though the interfacial phenomena were observed at LC-aqueous interfaces, in this system, the interface between LC and solid surface attracted attention recently as it induced the spontaneous formation of water droplets [51], thus there are much more room for further investigation. In short, LC-aqueous interfaces provide a promising class of biomolecular interfaces for reporting interfacial phenomena, combined with soft lithography techniques [52], it will have a wide range of innovative applications.

3 LC droplets

Instead of forming planar LC-aqueous interface, LCs can be emulsified to form LC droplets [53–63]. Nematic 5CB in liquid form at room temperature again becomes a good choice of making LC droplets/emulsions. Using polymer shells as templates [64] subsequently filled with LCs, emulsifying LCs by miniemulsion technique [65] or directly exploiting microfluidics [66] have been reported to produce LC droplets. Early studies focused on how the droplet size and interfacial compositions influenced the LC ordering configuration [64]. There are a number of general and important findings, with the same surface composition, LC droplets exhibited a size-dependent ordering transition. For large LC droplets ($\geq 3 \mu\text{m}$), LCs possess a bipolar configuration, with two point defects at two poles of the droplets. For small droplets ($\sim 700 \text{ nm}$), LCs possess a radial configuration, with a defect located at the center of the droplet. For the same size of LC droplets, LCs exhibit an adsorbate-driven ordering transition. LC droplets with initial bipolar configuration gradually changed to radial configuration as the increase of amount of amphiphilic molecules adsorbed onto LC droplets [37]. By taking advantage of this

responsive phenomenon, more recently, it was reported that LC droplets were used to detect bacteria and viruses [67]. The essential principle of detection was employing the interaction between lipids and LCs, as Gram negative bacteria (with outer membrane) and encapsulated viruses (with envelope) consisted of lipids, when contacting with LC droplets, lipids transferred to LC droplets, resulting in a radial configuration of LCs. This response provides an approach of screening bacteria and viruses based on their structural characteristics.

Last year, an interesting observation of using LC droplets to detect endotoxin from *E. coli* was reported [68]. Endotoxin is a lipid-polysaccharide comprised of a glycopospholipid, lipid A, shown in Figure 6(a). It was surprising to find that the concentration of endotoxin was extremely low (pg/mL) to induce a change in the ordering of the LCs from bipolar to radial (Figure 6(b)–(g)). The optical changes were striking and happened within a minute. It was confirmed that the ordering transition was not driven by adsorption of endotoxin over the surface of LC droplets, but instead by localization of the endotoxin at defects in LC droplets. Comparing to the current FDA-approved test for endotoxin, which is based on clotting the blood of horseshoe crabs, LC droplets based method is more friendly to animals and easy to operate. This system brings about new principles for sensing targeted biological species.

4 Conclusions and perspectives

This article focused on three aspects of employing LCs for bio/chemical detections and their advances in last ten years. The basis and advantage of LC-based assays undoubtedly contributes to unique properties of LCs: (1) molecular-level interactions at the interfaces can be amplified into ordering

Figure 6 (a) Schematic illustration of lipid A portion of endotoxin. Optical images and cartoon representation of LC droplets before ((b)–(d)) and after ((e)–(g)) exposure to endotoxin from *E. coli*. Reprinted with permission from [68]. Copyright 2011, Science.

transitions of LCs, the approach, therefore, does not require labeling of analyte; (2) one LC molecule can communicate and influence the ordering of adjacent LCs, consequently a nanoscale interruption of ordering propagates over microns, combined with the mobility of fluid-like LCs, the process can occur in seconds; (3) orientational changes in LCs can be simultaneously transduced into optical output, thus allowing transduction without the need of power or use of complex instrumentation; (4) the setup is simple and easy to operate, potentially useful for developing portable sensors or point-of-care testing.

The advances of design and engineering of solid substrates and functional molecules will bring more precise control over the LC ordering and the interfacial properties of both LC-solid and LC-aqueous interfaces, therefore, allowing further understanding of fundamental principles, eventually increasing sensitivity and specificity of detection. Whereas the commonly used nematic 5CB, other synthetic LCs and other phase (cholesteric) [69] or type (lyotropic) [70] of LCs offer a rich pool for exploration and provide more versatile properties. Taking advantage of emerging fabrication techniques, it is shown that low molecular weight LCs can be tailored to form a gel-like material with tunable mechanics [71], which promises a possibility of using LCs to culture mammalian cells (which are sensitive to substrate stiffness) [72] and reporting the interactions between cells and substrates. In addition, LCs with the orientational alignment and anisotropic mechanical properties might be a good candidate for directing neurite branching [73,74] and promoting stem cell differentiation, etc.

Overall, though LC-based sensors are still in its infancy, considering the high impact of LC displays in everyday life, it is not surprising if in future LCs bring another profound revolution, demonstrating their unimaginable applications and driving forward new research directions, again keep attracting spotlights in scientific world.

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- Reinitzer F. Beiträge zur kenntniss des cholesterins. *Montash Chem*, 1888, 9: 421–441
- Kumar S. *Liquid Crystals*. Cambridge: Cambridge University Press, 2001
- Woltman S J, Jay G D, Crawford G P. Liquid-crystal materials find a new order in biomedical applications. *Nat Mater*, 2007, 6: 929–938
- Hussain A, Pina A S, Roque A C A. Bio-recognition and detection using liquid crystals. *Biosens Bioelectron*, 2009, 25: 1–8
- Bai Y, Abbott N L. Recent advances in colloidal and interfacial phenomena involving liquid crystals. *Langmuir*, 2011, 27: 5719–5738
- Lowe A M, Abbott N L. Liquid crystalline materials for biological applications. *Chem Mater*, 2012, 24: 746–758
- Lagerwall J P F, Scalia G. A new era for liquid crystal research: Applications of liquid crystals in soft matter nano-, bio- and microtechnology. *Curr Appl Phys*, 2012, 12: 1387–1412
- Jerome R. Surface effects and anchoring in liquid crystals. *Rep Prog Phys*, 1991, 54: 391–451
- Gupta V K, Skaife J J, Dubrovsky T B, et al. Optical amplification of ligand-receptor binding using liquid crystals. *Science*, 1998, 279: 2077–2080
- Skaife J J, Abbott N L. Quantitative interpretation of the optical textures of liquid crystals caused by specific binding of immunoglobulins to surface-bound antigens. *Langmuir*, 2000, 16: 3529–3536
- Luk Y Y, Tingey M L, Dickson K A, et al. Imaging the binding ability of proteins immobilized on surfaces with different orientations by using liquid crystals. *J Am Chem Soc*, 2004, 126: 9024–9032
- Kim H R, Kim J H, Kim T S, et al. Optical detection of deoxyribonucleic acid hybridization using an anchoring transition of liquid crystal alignment. *Appl Phys Lett*, 2005, 87: 143901
- Govindaraju T, Bertics P J, Raines R T, et al. Using measurements of anchoring energies of liquid crystals on surfaces to quantify proteins captured by immobilized ligands. *J Am Chem Soc*, 2007, 129: 11223–11231
- Tan H, Yang S Y, Shen G L, et al. Signal-enhanced liquid-crystal DNA biosensors based on enzymatic metal deposition. *Angew Chem Int Ed*, 2010, 49: 8608–8611
- Shah R R, Abbott N L. Principles for measurement of chemical exposure based on recognition-driven anchoring transitions in liquid crystals. *Science*, 2001, 293: 1296–1299
- Yang K L, Cadwell K, Abbott N L. Mechanistic study of the anchoring behavior of liquid crystals supported on metal salts and their orientational responses to dimethyl methylphosphonate. *J Phys Chem B*, 2004, 108: 20180–20186
- Cadwell K D, Alf M E, Abbott N L. Infrared spectroscopy of competitive interactions between liquid crystals, metal salts, and dimethyl methylphosphonate at surfaces. *J Phys Chem B*, 2006, 110: 26081–26088
- Cadwell K D, Lockwood N A, Nellis B A, et al. Detection of organophosphorous nerve agents using liquid crystals supported on chemically functionalized surfaces. *Sens Actuators B*, 2007, 128: 91–98
- VanTrececk H J, Most D R, Grinwald B A, et al. Quantitative detection of a simulant of organophosphonate chemical warfare agents using liquid crystals. *Sens Actuators B*, 2011, 158: 104–110
- Pal S K, Acevedo-Velez C, Hunter J T, et al. Effects of divalent ligand interactions on surface-induced ordering of liquid crystals. *Chem Mater*, 2010, 22: 5474–5482
- Bi X, Lai S L, Yang K L. Liquid crystal multiplexed protease assays reporting enzymatic activities as optical bar charts. *Anal Chem*, 2009, 81: 5503–5509
- Chen C H, Yang K L. Detection and quantification of DNA adsorbed on solid surfaces by using liquid crystals. *Langmuir*, 2010, 26: 1427–1430
- Lai S L, Yang K L. Detecting DNA targets through the formation of DNA/CTAB complex and its interactions with liquid crystals. *Analyst*, 2011, 136: 3329–3334
- Chen C H, Yang K L. Functional protease assay using liquid crystals as a signal reporter. *Biosens Bioelectron*, 2012, 35: 174–179
- Chen C H, Yang K L. Liquid crystal-based immunoassays for detecting hepatitis B antibody. *Anal Chem*, 2012, 421: 321–323
- Lowe A M, Bertics P J, Abbott N L. Quantitative methods based on twisted nematic liquid crystals for mapping surfaces patterned with bio/chemical functionality relevant to bioanalytical assays. *Anal Chem*, 2008, 80: 2637–2645
- Bai Y, Abbott N L. Enantiomeric interactions between liquid crystals and organized monolayers of tyrosine-containing dipeptides. *J Am Chem Soc*, 2012, 134: 548–558
- Lockwood N A, Gupta J K, Abbott N L. Self-assembly of amphiphiles, polymers and proteins at interfaces between thermotropic liquid crystals and aqueous phases. *Surf Sci Rep*, 2008, 63: 255–293
- Brake J M, Daschner M K, Luk Y Y, et al. Biomolecular interactions at phospholipid-decorated surfaces of liquid crystals. *Science*, 2003, 302: 2094–2097
- Brake J M, Abbott N L. Coupling of the orientations of thermotropic

- liquid crystals to protein binding events at lipid-decorated interfaces. *Langmuir*, 2007, 23: 8497–8507
- 31 Brake J M, Abbott N L. An experimental system for imaging the reversible adsorption of amphiphiles at aqueous-liquid crystal interfaces. *Langmuir*, 2002, 18: 6101–6109
 - 32 Brake J M, Mezera A D, Abbott N L. Active control of the anchoring of 4'-pentyl-4-cyanobiphenyl (5CB) at an aqueous-liquid crystal interface using a redox-active ferrocenyl surfactant. *Langmuir*, 2003, 19: 8629–8637
 - 33 Lockwood N A, de Pablo J J, Abbott N L. Influence of surfactant tail branching and organization on the orientation of liquid crystals at aqueous-liquid crystal interfaces. *Langmuir*, 2005, 21: 6805–6814
 - 34 Bahr C. Surfactant-induced nematic wetting layer at a thermotropic liquid crystal/water interface. *Phys Rev E*, 2006, 73: 030702
 - 35 Price A D, Ignes-Mullol J, Vallve M A, et al. Liquid crystal anchoring transformations induced by phase transitions of a photoisomerizable surfactant at the nematic/aqueous interface. *Soft Matter*, 2009, 5: 2252–2260
 - 36 McCamley M K, Ravnik M, Arstenstein A W, et al. Detection of alignment changes at the open surface of a confined nematic liquid crystal sensor. *J Appl Phys*, 2009, 105: 123504–123507
 - 37 Gupta J K, Abbott N L. Principles for manipulation of the lateral organization of aqueous-soluble surface-active molecules at the liquid crystal-aqueous interface. *Langmuir*, 2009, 25: 2026–2033
 - 38 Lockwood N A, Cadwell K D, Caruso F, et al. Formation of polyelectrolyte multilayer films at interfaces between thermotropic liquid crystals and aqueous phases. *Adv Mater*, 2006, 18: 850–854
 - 39 Kinsinger M L, Sun B, Abbott N L, et al. Reversible control of ordering transitions at aqueous/liquid crystal interfaces using functional amphiphilic polymers. *Adv Mater*, 2007, 19: 4208–4212
 - 40 Gupta J K, Tjipto E, Zelikin A N, et al. Characterization of the growth of polyelectrolyte multilayers formed at interfaces between aqueous phases and thermotropic liquid crystals. *Langmuir*, 2008, 24: 5534–5542
 - 41 Kinsinger M I, Buck M E, Meli M V, et al. Langmuir films of flexible polymers transferred to aqueous/liquid crystal interfaces induce uniform azimuthal alignment of the liquid crystal. *J Colloid Interface Sci*, 2010, 341: 124–135
 - 42 Hartono D, Xue C Y, Yang K L, et al. Decorating liquid crystal surfaces with proteins for real-time detection of specific protein-protein binding. *Adv Funct Mater*, 2009, 19: 3574–3579
 - 43 Birchall L S, Ulijn R V, Webb S J. A combined SPS-LCD sensor for screening protease specificity. *Chem Commun*, 2008, 2861–2863
 - 44 Hartono D, Bi X, Yang K L, et al. An air-supported liquid crystal system for real-time and label-free characterization of phospholipases and their inhibitors. *Adv Funct Mater*, 2008, 18: 2938–2945
 - 45 Park J S, Abbott N L. Ordering transitions in thermotropic liquid crystals induced by the interfacial assembly and enzymatic processing of oligopeptide amphiphiles. *Adv Mater*, 2008, 20: 1185–1190
 - 46 Bi X, Hartono D, Yang K L. Real-time liquid crystal pH sensor for monitoring enzymatic activities of penicillinase. *Adv Funct Mater*, 2009, 19: 3760–3765
 - 47 Hartono D, Lai S L, Yang K L, et al. A liquid crystal-based sensor for real-time and label-free identification of phospholipase-like toxins and their inhibitors. *Biosens Bioelectron*, 2009, 24: 2289–2293
 - 48 Price A D, Schwartz D K. DNA hybridization-induced reorientation of liquid crystal anchoring at the nematic liquid crystal/aqueous interface. *J Am Chem Soc*, 2008, 130: 8188–8194
 - 49 Lockwood N A, Mohr J C, Ji L, et al. Thermotropic liquid crystals as substrates for imaging the reorganization of matrigel by human embryonic stem cells. *Adv Funct Mater*, 2006, 16: 618–624
 - 50 Yang Z Q, Gupta J K, Kishimoto K, et al. Design of biomolecular interfaces using liquid crystals containing oligomeric ethylene glycol. *Adv Funct Mater*, 2010, 20: 2098–2106
 - 51 Yang Z Q, Abbott N L. Spontaneous formation of water droplets at oil-solid interfaces. *Langmuir*, 2010, 26: 13797–13804
 - 52 Liu Y, Cheng D M, Lin I H, et al. Microfluidic sensing devices employing *in situ*-formed liquid crystal thin film for detection of biochemical interactions. *Lab Chip*, 2012, 12: 3746–3753
 - 53 Loudet J C, Richard H, Sigaud G, et al. Nonaqueous liquid crystal emulsions. *Langmuir*, 2000, 16: 6724–6730
 - 54 Prishchepa O O, Shabanov A V, Zyryanov V Y. Director configurations in nematic droplets with inhomogeneous boundary conditions. *Phys Rev E*, 2005, 72: 031712
 - 55 Heppenstall-Butler M, Williamson A M, Terentjev E M. Selection of droplet size and the stability of nematic emulsions. *Liq Cryst*, 2005, 32: 77–84
 - 56 Tjipto E, Cadwell K D, Quinn J F, et al. Tailoring the interfaces between nematic liquid crystal emulsions and aqueous phases via layer-by-layer assembly. *Nano Lett*, 2006, 6: 2243–2248
 - 57 Simon K A, Sejwal P, Gerecht R B, et al. Water-in-water emulsions stabilized by non-amphiphilic interactions: Polymer-dispersed lyotropic liquid crystals. *Langmuir*, 2007, 23: 1453–1458
 - 58 Zou J H, Fang J Y. Director configuration of liquid-crystal droplets encapsulated by polyelectrolytes. *Langmuir*, 2009, 26: 7025–7028
 - 59 Lopez-Leon T, Fernandez-Nieves A. Topological transformations in bipolar shells of nematic liquid crystals. *Phys Rev E*, 2009, 79: 021707
 - 60 Kinsinger M I, Buck M E, Abbott N L, et al. Immobilization of polymer-decorated liquid crystal droplets on chemically tailored surfaces. *Langmuir*, 2010, 26: 10234–10242
 - 61 Alino V J, Pang J, Yang K L. Liquid crystal droplets as a hosting and sensing platform for developing immunoassays. *Langmuir*, 2011, 27: 11784–11789
 - 62 Hu Q Z, Jang C H. A new strategy for imaging biomolecular events through interactions between liquid crystals and oil-in-water emulsions. *Analyst*, 2012, 137: 5204–5207
 - 63 Bera T, Fang J Y. Polyelectrolyte-coated liquid crystal droplets for detecting charged macromolecules. *J Mater Chem*, 2012, 22: 6807–6812
 - 64 Gupta J K, Sivakumar S, Caruso F, et al. Size-dependent ordering of liquid crystals observed in polymeric capsules with micrometer and smaller diameter. *Angew Chem Int Ed*, 2009, 48: 1652–1655
 - 65 Tongcher O, Sigel R, Landfester K. Liquid crystal nanoparticles prepared as miniemulsions. *Langmuir*, 2006, 22: 4504–4511
 - 66 Fernandez-Nieves A, Cristobal G, Garces-Chavez V, et al. Optically anisotropic colloids of controllable shape. *Adv Mater*, 2005, 17: 680–684
 - 67 Sivakumar S, Wark K L, Gupta J K, et al. Liquid crystal emulsions as the basis of biological sensors for the optical detection of bacteria and viruses. *Adv Funct Mater*, 2009, 19: 2260–2265
 - 68 Lin I H, Miller D S, Bertics P J, et al. Endotoxin-induced structural transformations in liquid crystalline droplets. *Science*, 2011, 332: 1297–1300
 - 69 Chang C K, Chiu S W, Kuo H L, et al. Cholesteric liquid crystal-carbon nanotube hybrid architectures for gas detection. *Appl Phys Lett*, 2012, 100: 043501
 - 70 Shiyanovskii S V, Schneider T, Smalyukh I I, et al. Real-time microbe detection based on director distortions around growing immune complexes in lyotropic chromonic liquid crystals. *Phys Rev E*, 2005, 71: 020702
 - 71 Agarwal A, Huang E, Palecek S, et al. Optically responsive and mechanically tunable colloid-in-liquid crystal gels that support growth of fibroblasts. *Adv Mater*, 2008, 20: 4804–4809
 - 72 Discher D E, Janmey P, Wang Y L. Tissue cells feel and respond to the stiffness of their substrate. *Science*, 2005, 310: 1139–1143
 - 73 Flanagan L A, Ju Y E, Marg B, et al. Neurite branching on deformable substrates. *Neuroreport*, 2002, 13: 2411–2415
 - 74 Yu L M Y, Leipzig N D, Shoichet M S. Promoting neuron adhesion and growth. *Mater Today*, 2008, 11: 36–43