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Surface Patterning via Thiol-Yne Click Chemistry: An Extremely Fast and Versatile Approach to Superhydrophilic-Superhydrophobic Micropatterns

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Superhydrophobic surfaces are characterized by extreme water repellency with water contact angles (WCA) greater than 150°, and a WCA hysteresis of less than 10°.[1,2] On the contrary, water spreads immediately on superhydrophilic surfaces leading to WCAs less than 10°.[3] Both superhydrophobicity and superhydrophilicity are the result of a combination of high surface roughness with either hydrophobic or hydrophilic material, respectively.[2] Combining these two extreme properties on the same surface in precise two-dimensional micropatterns opens exciting new functionalities and possibilities in a wide variety of applications from cell,[4–6] droplet,[5,7] and hydrogel microarrays[5,8] for screening to surface tension-confined microfluidic channels for separation and diagnostic devices.[9] A number of methods for making superhydrophobic-superhydrophilic micropatterns have been introduced over the past decade. For example, methods based on UV-induced decomposition of hydrophobic coatings on different substrates (alumina, TiO_2 film or SiO_2) were reported.[10] Photoinduced modificaiton of carbon nanotubes with hydrophilic azides,[11] plasma treatment,[12] microprinting,[13] or mussel-mimetic deposition of dopamine in combination with soft-lithography[14] have been described. In our previous work, we introduced a method based on UV-initiated photografting for making superhydrophobic-superhydrophilic micropatterns on porous polymer films.[4,15] Recently, Manna et al. reported an amine reactive superhydrophobic surface that permits post-fabrication by amine-functionalized molecules.[16] Most of the described methods, however, proceed slowly (e.g., 15 min irradiation time in the case of photografting),[4,15] lack the ability to easily tailor or modify the properties by different target functional groups, or require harsh conditions (e.g., plasma treatment or UV-induced decomposition), organic solvents (i.e., incompatible with aqueous conditions) and, therefore, cannot be directly applied to make patterns of biomolecules. These limitations restrict the range of possible practical applications of produced superhydrophobic-superhydrophilic micropatterns. Developing a universal method that is facile, versatile, as well as provides good optical and chemical surface properties remains a big challenge.

To meet this challenge, here we present an extremely fast (<15 s), initiator-free surface modification method compatible with aqueous conditions for creating superhydrophobic-superhydrophilic micropatterns using thiol-yne "click" chemistry[17] (**Figure 1**A). Phototriggered thiol-yne reactions have been explored as a viable approach to surface modifications, such as using different thiols to modify "yne"-containing polymer brushes,[18] immobilizing gold nanoparticles on a polymer surface site-specifically,[19] and creating micropatterns on a monolayer by microcontact printing.[20] To our knowledge, however, this type of functionalization strategy has never been applied to create superhydrophobic-superhydrophilic micropatterns. Here we show that an alkyne functionalized porous polymethacrylate surface could be easily transformed into either a superhydrophobic or superhydrophilic surface under UV irradiation. We show that the reaction is extremely fast and requires as little as 0.5 s of UV irradiation in the presence of an initiator and only 5 s without any initiator. The functionalization can be performed in various solvents including water (Figure 1) allowing to pattern biomolecules. In this way, superhydrophobic-superhydrophilic micropatterns incorporating different orthogonal reactive functional groups (e.g., OH, NH_2, or COOH) could be created using this method. An application of the produced superhydrophobic-superhydrophilic structures to pattern cells as well as the use of the thiol-yne photo-click method to pattern cysteine-containing peptides are presented.

To fabricate a nanoporous polymer layer modified with alkyne groups (Figure S1), we used a 12.5 µm-thin porous polymer layer of poly(2-hydroxyethyl methacrylate-*co*-ethylene dimethacrylate) (HEMA-EDMA) prepared on a glass substrate according to previously published procedure.[4] The resulting HEMA-EDMA polymer layer has high surface roughness (50% porosity and 80–250 nm pores based on SEM, Figure S2) and is highly wettable with static (θ_{st}), advancing (θ_{adv}) and receding (θ_{rec}) WCAs close to ~4.2°, 7.1° and 0°, respectively (Figure S2). The HEMA-EDMA surface was modified with 4-pentynoic acid

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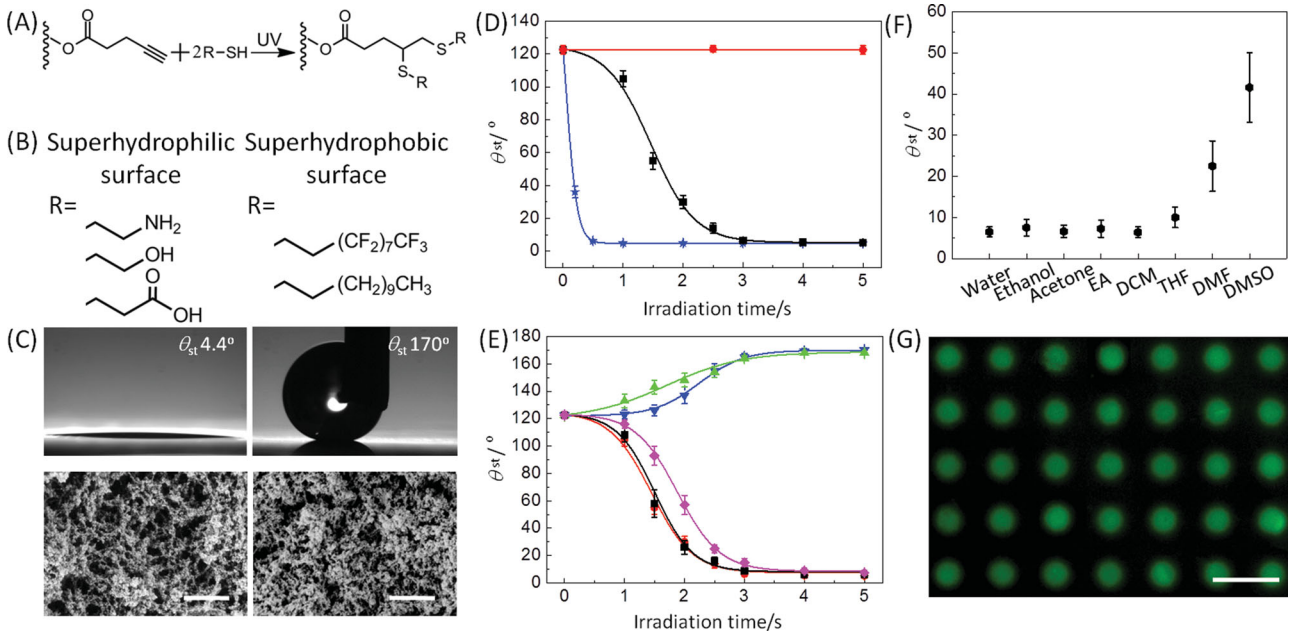

Figure 1. (A) Schematic representation of the alkyne surface modification via UV-induced thiol-yne click chemistry; (B) Examples of thiols used for the formation of either superhydrophilic or superhydrophobic surfaces; (C) Water droplet on a cysteamine-modified superhydrophilic surface (left) and on a 1*H*,1*H*,2*H*,2*H*-perfluorodecanethiol modified superhydrophobic surface (right), and SEM images of the corresponding porous polymers. (D,E) Kinetics of the alkyne surface modification using the thiol-yne click chemistry. The θ_{st} of the polymer layer modified using: (D) cysteamine with (blue) or without (black) photoinitiator 2,2-dimethoxy-2-phenylacetophenone (DMPAP) and with DMPAP but without UV irradiation (red); (E) cysteamine (black squares), 3-mercaptopropionic acid (red circles), 2-mercaptoethanol (purple diamonds), 1*H*,1*H*,2*H*,2*H*-perfluorodecanethiol (blue triangles), and 1-dodecanethiol (green triangles) without DMPAP upon UV irradiation. (F) θ_{st} of the alkyne surfaces functionalized using 3-mercaptopropionic acid dissolved in different solvents; no photoinitiator; 5 s UV irradiation. Results from 3 different samples and two measurements per sample. (G) Fluorescence microscope image of a fluorescein-ß-Ala-GGGGC peptide pattern prepared by the thiol-yne reaction on the alkyne porous surface carried out in aqueous solution. Scale bars: 1 µm (C) and 500 µm (G).

by a standard esterification procedure (supplementary information). The analysis of the WCA variation over time and within the depth of the polymer film verified that the modification proceeded completely throughout the thickness of the polymer layer after 4 h of the reaction time (Figure S3). The θ_{st} of the polymer surface increased from 4.2° to 124° after the esterification. The intense peak at 2120 cm^{-1} in the Raman spectrum (Figure S4) also confirmed the presence of terminal alkyne groups.[19] After surface modification, the polymer layer maintained its porous structure and did not show significant changes of the morphology (SEM in Figure S2). Due to the small size of the pores,[21] the light scattering on the wetted polymer layer is reduced leading to more than 90% transmittance of visible light (Figure S5). The resulting alkyne porous polymer can be functionalized via the thiol-yne click reaction to transform the surface either into a superhydrophobic or superhydrophilic surface depending on whether a hydrophobic or hydrophilic thiol being used (Figures 1B-C). As a general procedure, the porous alkyne surface is wetted with a thiol solution, covered with a quartz slide and irradiated with 260 nm UV light (12 $mW \cdot cm^{-2}$) at room temperature.

In general, long UV irradiation times can lead to oxidation and degradation of the substrate as well as to the damage of biomolecules used for functionalization. Most of the existing UV-based techniques for the formation of superhydrophobic-superhydrophilic patterns require irradiation times ranging from several minutes to several hours, which limits possible applications of such methods.[10,15] On the other hand, functionalization of the alkyne-surface with cysteamine using the thiol-yne reaction required as little as 0.5 s of UV irradiation in the presence of 2,2-dimethoxy-2-phenylacetophenone (DMPAP) as a photoinitiator to transform the hydrophobic alkyne polymer (θ_{st} = 124°) into a superhydrophilic surface (θ_{st} = 4.4°) (Figure 1D). The same reaction without the photoinitiator required only 5 s for the functionalization and no reaction happened without UV light. The thiol-ene reaction without a photoinitiator was reported previously by Cramer et al.[22] Without UV irradiation, however, the WCAs of the surface did not change at all even in the presence of the photoinitiator, indicating that there was no physisorption of the thiols on the surface.

Figure 1E shows the fast kinetics of the initiator-free surface modification as well as the ability to use different thiols to create either superhydrophobic or superhydrophilic surfaces. Modification of the surface with hydrophobic 1-dodecanethiol or 1*H*,1*H*,2*H*,2*H*-perfluorodecanethiol endows the porous surface with superhydrophobicity (θ_{adv}, θ_{st} and θ_{rec} being as high as 171°, 169° and 162°, or 173°, 170°, and 164°, respectively). In the Raman spectra, sharp decline of the alkyne bands (~2120 cm^{-1}) was observed (Figure S6). No sign of the vinyl sulfide species (~1657 cm^{-1}) was detected (Figure S7), indicating full conversion of the alkyne groups to the 1,2-dithioether adduct.[21] Figure S8 shows the stability test of superhydrophobic surfaces. The static WCAs of the surfaces in air, PBS buffer, and acetic

and basic water solutions (pH = 5 and 10) remained above 160° after 120 h incubation. Due to the protein adsorption, the WCA of the surface decreased in DMEM solution containing 10 vol% FBS. The porous structure of the HEMA-EDMA polymer layer plays an important role in fabricating superhydrophobic or superhydrophilic surfaces. Using the thiol-yne reaction under the same conditions, the functionalization of an alkyne-modified non-porous HEMA-EDMA surface with cysteamine leads to a decrease of θ_{st} from 63° to 44° and the functionalization with *1H,1H,2H,2H*-perfluorodecanethiol leads to an increase of θ_{st} from 63° to 110° after 5 s UV irradiation.

The ability to perform the thiol-yne surface functionalization in different both apolar and polar solvents including water can increase the number of possible thiols applicable for the functionalization. Water is especially interesting in terms of its environmental impact, low cost and the compatibility with thiol-containing biomolecules, such as proteins or peptides. To test the ability to use the thiol-yne-based surface functionalization in different solvents, we modified the alkyne HEMA-EDMA surface with 3-mercaptopropionic acid dissolved in several common solvents (Figure 1F). Based on the water contact angle measurements, the reaction proceeded extremely fast in ethanol, acetone, ethyl acetate, DCM, THF and water. The hydrophobic alkyne-modified polymer could be transformed into the superhydrophilic surface after only 5 s of irradiation. The reaction in DMF and DMSO required 15 s of the irradiation to make the surface superhydrophilic. The fact that the reaction proceeds well in water and without an initiator can

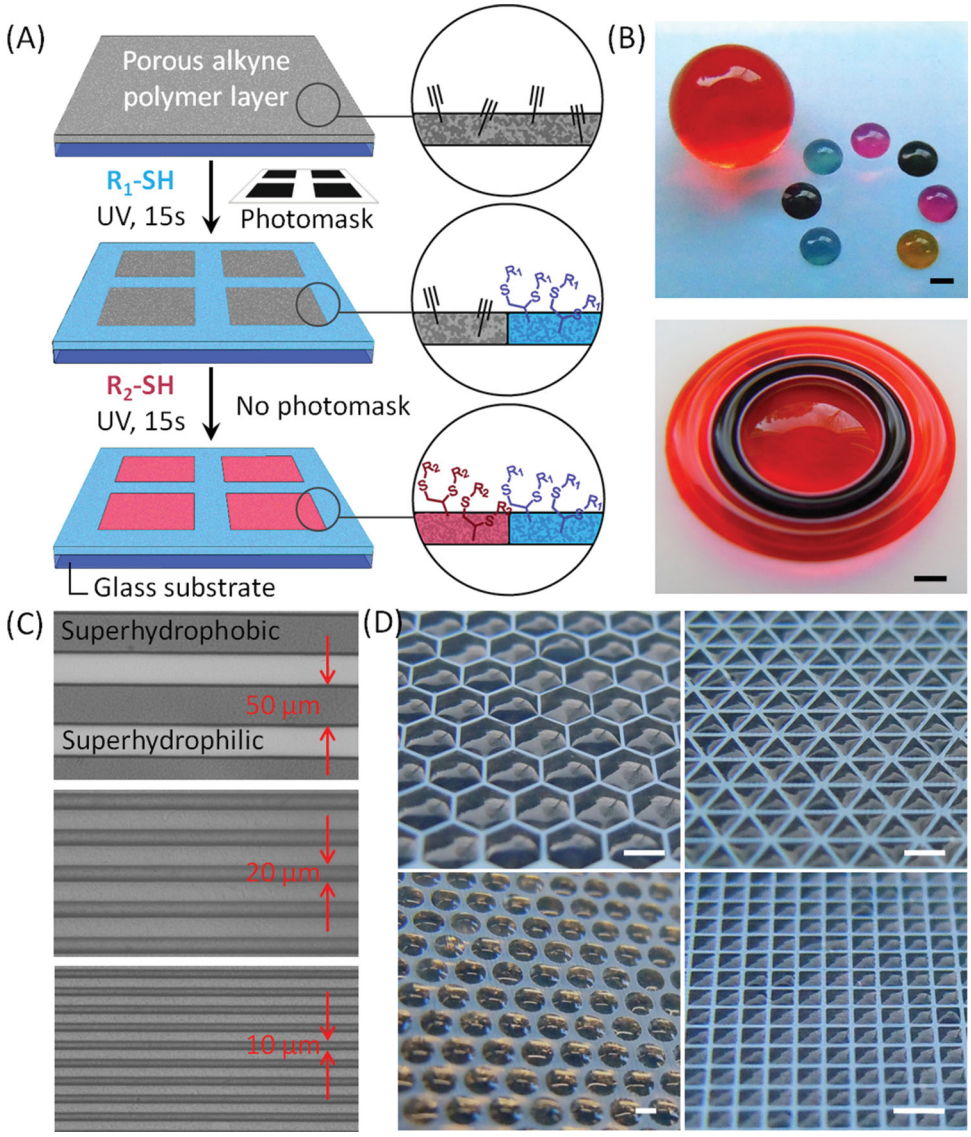

Figure 2. (A) Schematic representation of the thiol-yne photo-click reaction for creating superhydrophobic-superhydrophilic micropatterns using the alkyne-modified porous polymer layer as a substrate. Optical images of (B) superhydrophilic-superhydrophobic patterns filled with dye water solutions; superhydrophobic gap between the two rings is 100 µm; (C) Superhydrophilic regions (light areas) separated by superhydrophobic gaps (dark areas) of different widths; (D) DropletMicroarrays formed by dipping the superhydrophobic-superhydrophilic arrays with different geometries into water. Wetted parts become transparent (dark). Scale bars are 1 mm.

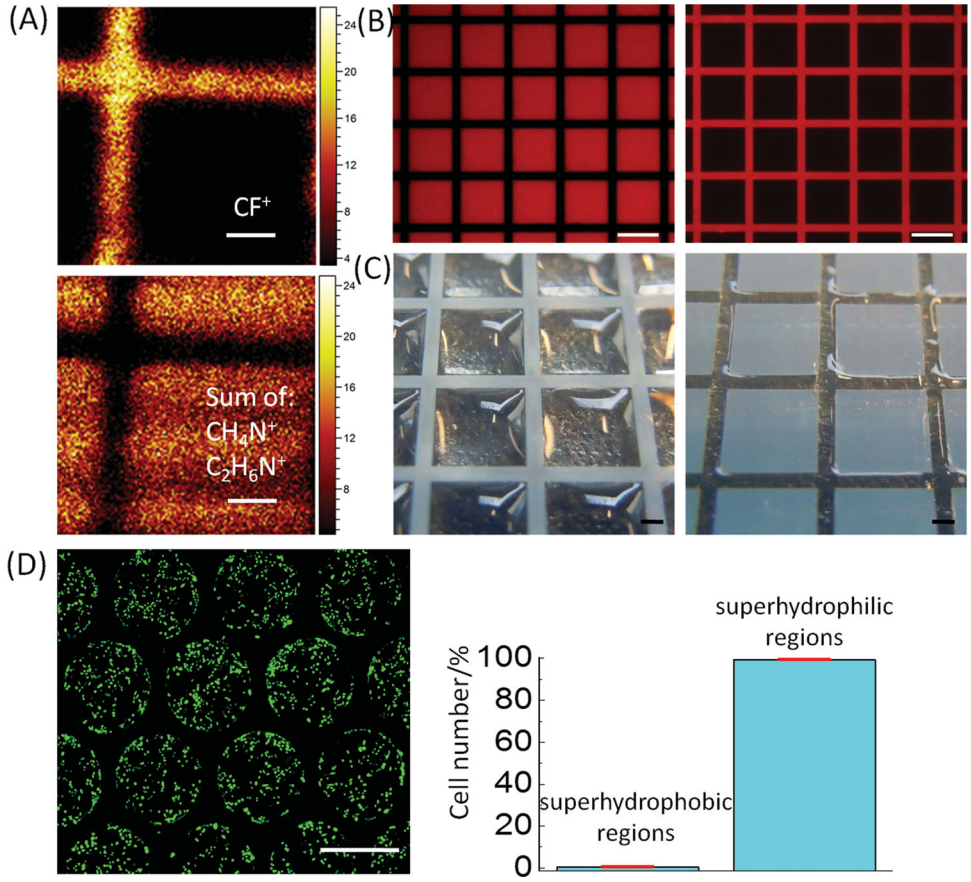

Figure 3. (A) ToF-SIMS 2D graphs of positive CF^+-ion and the sum of CH_4N^+ and $C_2H_6N^+$-ions, showing the patterning of 1*H*,1*H*,2*H*,2*H*-perfluorodecanethiol and cysteamine, respectively. (B) Fluorescence microscope images showing the inverse superhydrophobic-superhydrophilic patterns filled with aqueous solution of Rhodamine B; (C) The superhydrophilic regions of inverse superhydrophobic-superhydrophilic patterns filled with water. Inverse patterns produced using the same photomask by switching the order in which the hydrophobic and hydrophilic regions were created; (D) Fluorescence microscope images of Hela-GFP cells after growing for 48 h on a superhydrophobic-superhydrophilic array, showing the preferential adherence of cells on superhydrophilic spots and less than 1% occupation on the superhydrophobic barriers. Scale bars are 100 μm (A), 300 μm (B) and 1 mm (C and D).

be important for the rapid functionalization of such surfaces with biomolecules. This has been shown by patterning a fluorescein-ß-Ala-GGGGC peptide containing a terminal cysteine residue on the alkyne functionalized HEMA-EDMA surface (Figure 1G). The pattern was prepared by irradiating the alkyne surface wetted with an aqueous solution of the peptide (0.25 mg/L) during 15 s.

The advantage of using a reactive surface for patterning is that the non-irradiated areas remain reactive after the first step of patterning and can be subsequently modified to create patterns of a secondary functionality. Importantly, the second step of modification does not require a photomask as a reactive alkyne pattern is generated during the first step of irradiation through a photomask. **Figure 2** shows schematically the process for creating superhydrophobic-superhydrophilic micropatterns. First, the alkyne porous layer is wetted with an acetone solution containing 5 vol% 1*H*,1*H*,2*H*,2*H*-perfluorodecanethiol and irradiated with UV light through a photomask yielding a pattern of superhydrophobic as well as reactive alkyne areas (Figure S9). After removing the photomask and washing with acetone, the whole surface is subjected to a second thiol-yne reaction with cysteamine hydrochloride (15 wt% ethanol solution), leading to the modification of unreacted alkyne groups and the formation of a superhydrophobic-superhydrophilic pattern. It is worth nothing that θ_{rec} on the superhydrophobic areas decreased by only 2° after the second modification step.

Figures 2B shows examples of well-defined superhydrophobic-superhydrophilic patterns of different sizes and geometries prepared by this method. Multicomponent patterns with feature sizes as small as 10 μm (Figure 2C) could be produced. Using the method from Ueda et al.,[5] it is possible to create high-density arrays of completely separated microdroplets (DropletMicroarray approach) on the produced superhydrophobic-superhydrophilic patterns (Figure 2D). Due to the reduced light scattering, the superhydrophilic nanoporous polymer layer becomes transparent when wetted with water (Figure S3), allowing easier discrimination of spots and facilitating the use of inverted microscopes.

To further improve this method and to avoid possible modification of the residual alkyne groups remaining after the first irradiation step, we used an ethanol-water (1:1) solution instead of pure ethanol to dissolve cysteamine. In this case, the contact

angle (θ_{st}) of the ethanol-water solution on the alkyne-functionalized and the fluorinated surfaces was 0° and 135 ± 3°, respectively. Thus, the cysteamine solution could only wet the alkyne-functionalized areas (θ_{st} = 0°), while the fluorinated areas remained dry (Figure S9). This simple method completely prevents immobilization of the thiol on the superhydrophobic areas during the second functionalization step. This was confirmed by time-of-flight secondary ion mass spectrometry (ToF-SIMS) (**Figure 3**A).

Another advantage of this sequential surface modification method is that inverse patterns can be obtained simply by switching the order of the two chemicals in the patterning procedure (Figure 3B-C and S10A). The grids of water microchannels on the inverse patterns shown in Figure 3C (right) can be used, for example, as barriers for confining water immiscible organic solvents in the hydrophobic spots (Figure S10B).

Finally, we show that the produced superhydrophobic micropatterns show excellent cell repellent properties superior to those produced by a previously described photografting technique.[4,23] To visualize this, Hela-GFP cells were seeded on an array of superhydrophilic spots and superhydrophobic barriers and incubated for 2 days. Figure 3D and Figure S11 show that cells adhered well to the superhydrophilic microspots, demonstrating the biocompatibility and nontoxicity of the surface, however, less than 1% of cells occupied the superhydrophobic regions separating the microspot areas after 2 days of culture.

In conclusion, we have developed an extremely fast initiator-free method based on the thiol-yne click chemistry for the rapid fabrication of superhydrophobic-superhydrophilic micropatterns. The method can be applied to a variety of different functional molecules, containing, for example, unprotected OH, NH_2 or COOH groups, as long as a terminal thiol group is present. Thus, functional and/or reactive superhydrophobic and superhydrophilic micropatterns can be created. We also showed that the patterning could be performed in aqueous conditions, making this method useful for biological applications, where rapid transformation and benign aqueous conditions are crucial. Given the swiftness, versatility, mild reaction conditions, as well as compatibility with various chemistries and solvents, we believe that this method will find numerous applications for creating multifunctional superhydrophobic-superhydrophilic micropatterns.

Experimental Section

Materials and Methods are provided as Supporting Information.

Supporting Information

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

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