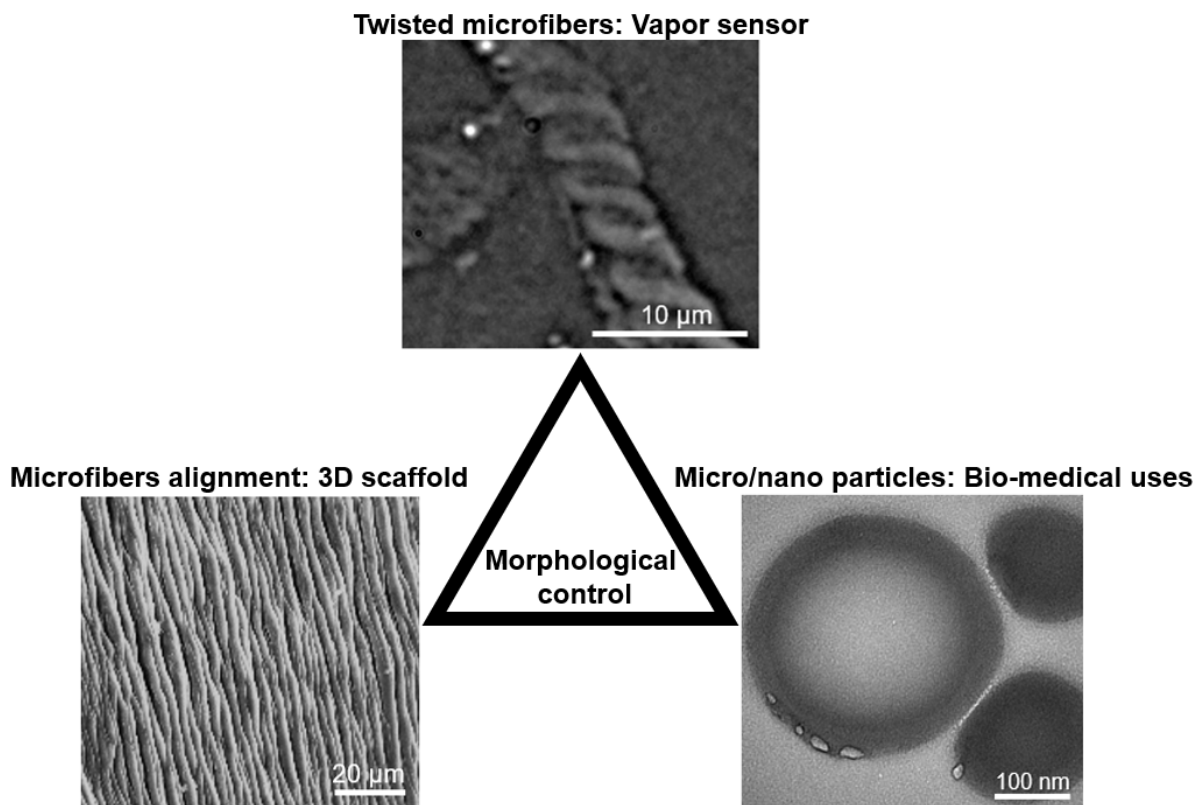


Title	自己組織化巨大多糖類の形態制御
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Citation	
Issue Date	2021-09
Type	Thesis or Dissertation
Text version	ETD
URL	<a href="http://hdl.handle.net/10119/17536">http://hdl.handle.net/10119/17536</a>
Rights	
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学位記番号	博材第 523 号		
学位授与年月日	令和 3 年 9 月 24 日		
論文題目	Morphological control of self-organized body on supergiant polysaccharides		
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### 論文の内容の要旨



### Graphical abstract

In materials design, the relationship between polymer morphology and physical properties is crucial. The researchers are attempting to utilize alternative materials such as natural biopolymers to limit the consumption of non-renewable resources produced by synthetic materials. In recent decades, there has been an increased interest in the utilization of polysaccharides, particularly bioactive ones, for various novel applications owing to their biocompatibility, non-toxicity, and some specific therapeutic activities. The biological activities of polysaccharides are strongly affected by their chemical structure and chain conformations. The morphological control of polysaccharides from nano to micrometer scale has seldom been utilized in vitro because

of the difficulties in regulating self-assembled structures. Herein, it is demonstrated that a cyanobacterial polysaccharide, *sacran*, could hierarchically self-assemble as twisted fibers from the nanoscale to microscale with diameters of  $\sim 1 \mu\text{m}$  and lengths  $>800 \mu\text{m}$ , that are remarkably larger than polysaccharides previously reported. Unlike other rigid fibrillar polysaccharides, the *sacran* fiber was capable of flexibly transforming into two-dimensional (2D) snaking and three-dimensional (3D) twisted structures at an evaporative air-water interface. It was determined that the microfiber had a diameter of  $\sim 1 \mu\text{m}$  and formed of a self-assembled torsional structure of nanofibers with diameters of  $\sim 50 \text{ nm}$ . This structure was stable in pure water. Upon adding monovalent cations such as  $\text{Na}^+$  from  $\text{NaCl}$ , the microfiber is capable of disassembling into submicrometer-scale particles. The microfibrils tended to integrate into a uniaxially oriented state along the contact line of the evaporative air-water interface. When one side of the microfibrils was fixed, they drastically transformed into 2D snaking and 3D twisted structures. The velocity of the contact line movement during drying affected the structure formed because of the capillary forces at work between the microfibrils. The evaporative air-water interface also induced multi-twisted structures to form from multiple microfibrils, thereby showing that this material has self-similar nano and microstructures. The snaking and twisted fibers made possible a film exhibiting millisecond-response repulsive motion to water vapor. By introducing functional molecules into the microfiber, it would be possible to prepare a variety of soft actuators responding to other changes in the external environment, such as light, pH, and temperature. The method for preparing vapor sensors developed by this study not only improves understanding of how the motion of self-assembled structures responds to stimuli but also contributes towards the design of environmentally adaptive materials with a high potential for sustainable use. We envision that this approach is capable of reconstructing additional natural materials towards developing advanced microsensors. Moreover, the scaffold of highly oriented M-fibers was successfully prepared. This could be an excellent place to start looking into cell orientation in relation to M-fibers for the new material design.

Moreover, the deformation process of *sacran* microfiber to nano-micro particles was also clarified in vice versa. The interaction between polymer chains is an essential component in studying *sacran* morphological change. The microfibrils deformed to particles by reducing the intermolecular interaction, for example, the dilution and the salination. In case of decreasing concentration to the semi-diluted state ( $c < c_e 0.015 \text{ wt}\%$ ), the polymer would be in the unentangled state which is unable to form microfiber. At the concentration of  $0.010 \text{ wt}\%$ , the microfibrils significantly deformed into the nanofibers and nanofragments. This could be the boundary concentration of nano to micro assembling process. After that, the salination effect was studied as another factor that suppresses the interaction between the polymer chains. *Sacran* at a diluted state ( $0.001 \text{ wt}\%$ ) with  $10 \text{ mM}$  of  $\text{NaCl}$  added, the salting-in affected on higher solubility of polymer chains. Then,  $100 \text{ mM}$  of  $\text{NaCl}$  was added, the salt affected on less soluble of the polymer referred to the salting-out. This effect could produce the *sacran* particles with a very narrow size distribution. However, the dilution and the salination method conferred a small quantity of particles because

the particle would be formed with narrow size distribution under a very low polymer concentration or with a crucial high concentration of salt. That problem could be overcome by the ultrasonication technique. At polymer concentration 0.010 wt%, the *sacran* microparticles are successfully prepared. Sonication plays a vital role in polymer scission and spherical shape formation through cavitation. The overall treated ultrasonic energy directly affects the size of the particles. Consequently, the polymer particles were annealed, aiming to get microparticles gel for further applications. For instance, the *sacran* microgel represented super-moisturizing ability comparative to other currently used materials. This would be a significant investigation of a new polysaccharide particle because the preparation processes are ultimately simple and non-necessity of organic solvents nor artificially synthetic molecules, they would be the alternative option in the green chemistry. Furthermore, the Sacran microparticles could be modified for additional applications such as microgel drug carrier or intranasal spray for moisture maintaining. Based on the outstanding properties of the prepared, this study could lead to a new material design for medical purposes in the future.

**Keywords:** Polysaccharides, self-assembly, fibers, particles, drying.

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#### 論文審査の結果の要旨

天然多糖は環境中に最も多く存在する天然高分子である一方、その構造はあらゆる高分子の中で最も複雑であり、その組織化挙動はほとんど解明されていない。一方、日本固有のラン藻である *Aphanothece sacrum* から効率よくサクランという超巨大細胞外多糖が得られることが見出されてきた。本研究では、サクランを題材に乾燥濃縮過程で形成される様々な自己組織化体の形状・構造コントロールを行うことを目的とし以下の研究を進めた。

第一章では、高分子電解質の自己組織化、多糖、サクランに関する研究背景を述べ、従来報告されてきた論文をレビューすることで、本論文の位置づけを行い、目的、意義を述べた。

第二章では、サクラン水溶液一滴がガラス基板の上で乾燥するときに形成される自己組織化体の形状

変化を調べた。乾燥痕の中には中央の結晶用の析出物とその周辺に存在するらせん状構造体および縁に存在する高度集積物に分類できることが分かった。特にらせん状構造体に関し、二次元にスネーキングするものと三次元にツイストするものが混在し、これらは乾燥速度や添加塩濃度で制御できることが分かった。しかも、このらせん状構造体を含むフィルムは湿度に反応して瞬時に形状を変化させるアクチュエータとしても機能することが見出された。さらに、このらせん構造体を並列させたところにhMSCヒト幹細胞を播種したところ構造体の長軸に沿って細胞が進展する現象が見られたことを付記した。

第三章では、サクランに超音波を照射することで形成するナノ構造体の階層構造制御に関して議論した。マイクロスケールの繊維束を形成したサクランに超音波照射を施すと、より短いマイクロ繊維となり、続いてマイクロ球状構造体へと変化した。この球状構造体に塩の添加および脱塩を繰り返すことで形状を変化させることに成功した。また、さらに加熱処理により架橋を施し球状構造体を安定化した後、そこに含まれる結合水の量を評価した結果、加熱処理により飛躍的に結合水量が増加することが分かった。これにより保水力も高まり、緑化資材などの保水性を活用した応用も見越せるようになった。

第四章では、全ての章を総括し、サクランという超巨大細胞外多糖が作る自己組織化体の形状制御に関し纏めて説明した。

以上、本論文は天然高分子である多糖が階層的に組織化体を形成することを見出し、その応用も提案するなど学術的に貢献するところが大きい。よって博士（マテリアルサイエンス）の学位論文として十分価値あるものと認めた。