

# Triggered, Nanostructured Biodegradables (TNBs) for Surgical Implants

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**Abstract:** In medicine, objects that need to be removed later - such as stents - are commonly placed in patients, with the time of removal dependent on progress of the patient. In these cases biodegradable materials that last for a specific time may not be suitable. We propose a new class of nanostructured materials that can hold their form as long as wanted, Triggered, Nanostructured Biodegradables (TNBs), that can be disintegrated to micro- or nanoscaled components when externally triggered on command to do so. DNA nanotensegrity microstructures, metastable foams, nanobots and other bioinspired disintegratable scaffold structures are given as potential examples.

**Keywords:** Triggered nanostructured biodegradables, surgical implants, stents, tensegrity, nanobots, modular nanobot dental braces, tektites, Prince Rupert's drops.

## INTRODUCTION

Surgeons frequently implant materials in the body that need to come out at a later date. If the material is not biodegradable, then in present practice this requires an additional surgical procedure to remove it, with attendant risks. An example where one would not want an ordinarily biodegradable material is the stent:

- 1 The time it is to be left in place may not be determinable in advance.
- 2 Gradual biodegradation could lead to counterproductive transient blockage.

For example, an increase in bilirubin after placement of a stent in the common bile duct would suggest that the stent itself has become occluded [1], perhaps due to bile glycoprotein mucin [2]. Weaning from shunts [3] also suggests their removal after an unpredictable time. It would therefore be an advance to have a material whose degradation were instantaneous, complete, and triggered on command. We call such a material a Triggered, Nanostructured Biodegradable (TNB).

If a stent has done its job, ordinary biodegradability might lead to transient pieces that would block the duct, a counterproductive outcome, and even if not, the time course of biodegradation may not match the patient's needs. Complications of stents sometimes requiring their premature removal include infection [4], thrombosis [5], perforation [6] stent migration [7] and unplanned stent supercoiling [8]. "Potential complications with removal include tracheal disruption, retained stent pieces, mucosal tears, re-obstruction requiring new stent placement, the need for postoperative ventilation, pneumothorax, damage to the pulmonary artery, and death" [9]. Nonmechanical risks of ordinary biodegradable stents [10] include restenosis [11] and thrombosis [12].

Tektites are natural glass objects that form on meteorite impact [13]. Rock is melted into splashed molten drops because of the huge impact energy. These cool rapidly, a process called quenching. Their natural shapes include "spheres, oblate ellipsoids, dumbbells, teardrops, and tori" [14]. Some of them are unstable: the slightest scratch will cause them to explode to dust (Edward Anders, personal communication, 1962; cf. [15]). This phenomenon, called Prince Rupert's drops, has been known for 350 years [16] and has been extensively investigated using rapidly cooled glass drops [17]. Tektites then show that at least one real material exists whose degradation is instantaneous, complete, and triggered on command.

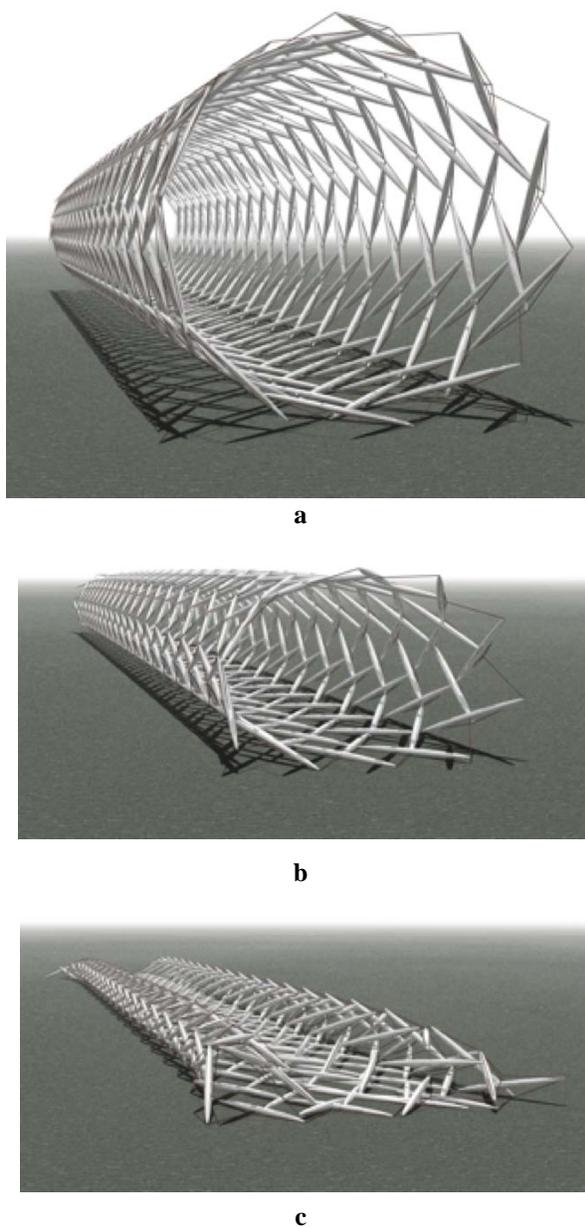
We could broaden the concept to consider materials that have two states, with a transition between them that can be triggered on command. For example, materials with "memory" of a previous state can be triggered to return to that state. Such materials are being used in surgery and prosthesis, but, of course, only change shape rather than disappear [18].

It may be possible to build TNBs as tensegrity structures. These were originally designed with their stability properties in mind:

"The word 'tensegrity' is an invention: a contraction of 'tensional integrity.' Tensegrity describes a structural-relationship principle in which structural shape is guaranteed by the finitely closed, comprehensively continuous, tensional behaviors of the system and not by the discontinuous and exclusively local compressional member behaviors. Tensegrity provides the ability to yield increasingly without ultimately breaking or coming asunder" [19].

However, tensegrity structures are only stable for certain ranges of their parameters. A change in one of these parameters could lead to collapse of the whole structure [20] (Fig. 1). There are models for collapsible tensegrity scaffoldings [21], tensegrity extendable bridges [22], and the Hoberman

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**Fig. (1).** Example for (a) a tensegrity, (b) a partially collapsed version of same, (c) a fully collapsed version. Images reproduced with kind permission of Gerald de Jong [62].

sphere [23]. Higher energy metastable tensegrity structures have been demonstrated [24], and such tensegrity metastability was hypothesized for the cell state splitter that may trigger cell differentiation in embryos [25]. Manufacturing collapsible tensegrity structures with microscale components would give them practical application. While tensegrity structures may not be stiff enough for most engineering constructs, they might be perfect for biological applications: artificial limbs and bracing at one scale, stents and the like at another.

It is actually rather difficult to design a tensegrity structure that retains a three dimensional shape [26]. Thus alteration of a tensegrity structure to make it collapse may be quite feasible.

Scaffolds could be built from micro- and nano-Origami structures, such as the DNA box with DNA triggered lid [27] or the DNA tetrahedron container [28], or nano-Origami structures made from stressed material, that, when the signal comes, collapses (actuates) [29]. Progress has been made towards large structures based on the “DNA tensegrity triangle” [30]. DNA nanomachines [31] present an opportunity to build larger structures that could disintegrate “on command”. For example, the DNA could be chosen to contain the sequences broken by specific endonucleases. The flooding of the stent with an endonuclease solution could be the trigger for disintegration. Now that we can make artificial restriction enzymes [32], it may be possible to guarantee nontoxicity with the right stent DNA material/endonuclease combination.

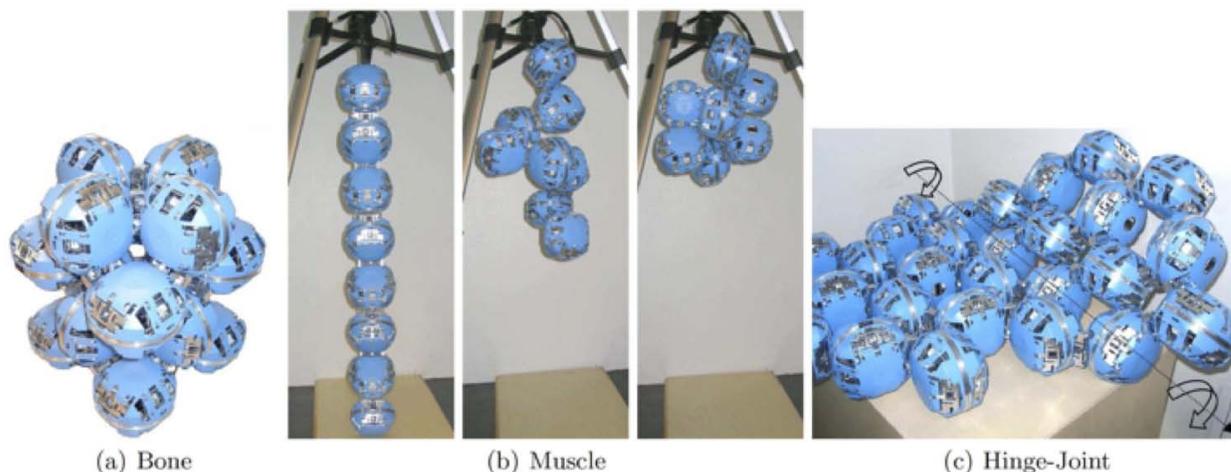
Click-stop mechanisms, where the structure that ensures the “stop” disintegrates with the trigger, would be feasible. A click-stop mechanism has been found in the diatom *Corethron pennatum* [33].

We can also think about structures that are inert and would leave the body and where only the connections are made from the “triggered material” – this would give us a smart nano/microcomposite. A hierarchical material could be envisaged where the highest level of hierarchy is ensured by the triggerable material, and when the trigger comes, the whole collapses to smaller structures that can easily leave the body.

Modular robots [34] are presently macroscopic devices, whose unit robots combine or work together in many configurations (Fig. 2). One of those configurations, generally not considered, would be for all robots to disconnect. Modular nanobots [35] could thus become a basis for structures that not only disintegrate on command, but perhaps also change configuration on demand while they are still needed. For example, braces for teeth require frequent manual adjustment, which could be done instead, perhaps automatically, by modular nanobot braces.

The oscillations in tensegrity icosahedrons [36] switch them from left handed to right handed spirals. Perhaps we could make a material that is not attacked by the immune system or enzymatically digested when it has one chirality, and that is attacked or digested when it has the other chirality. The transition between these two states would have to be triggered.

For stents outside the circulatory system, such as bile ducts, ureters, etc., changing the stent from a stiff, inert structure to a collapsed and readily passed material might be as simple as changing the phase of some of its components. Many tissues in the body, for example, muscles, undergo phase transitions, much like water into ice [37]. Usually this is related to calcium ion shifts or shifting chirality. If constructed from carbon nanotubes and collagen in some form that could undergo a phase transition, for instance, the stent could disintegrate into inert components. Intravascular stents are more of a challenge. They must be relatively inert, and readily phagocytized or removed from the circulatory system upon collapse without disrupting the system, causing clots or tissue damage. If the tensegrity stent is constructed from nanotubes, they are needle-like and could pass through the



**Fig. (2).** Three structural modifications of the modular ATRON robot. (a) The bone configuration with high structural strength, (b) the muscle configuration made from 8 ATRON modules that contracts by forming a compact helix shape and (c) the hinge-joint with one degree of freedom. From [34d] with permission. On command, all robots could disengage from one another simulating a logical TNB.

walls of blood vessels without harm. Magnetic nanotubes [38] could reside in the soft tissues and be pulled out of harms way. An alternative is that the stent components could be directed to an arteriole that could be safely blocked.

Gels made of networks of polymers, such as hyaluronan [39], could be triggered [40] to undergo a sol/gel transition by either altering the lengths of the polymers, which could suddenly change their connection properties below the critical percolation bond probability [41], or by altering the ionic conditions so that the ratio of hydrophobic/hydrophilic contacts between polymers changes. A further possible material would be polysaccharides such as cellulose.

Another approach is to make implants out of a rigid foam that can be liquefied on command. For example, the foam might be a stabilized emulsion that breaks when a particular (biocompatible) reagent is introduced. A stiff emulsion of two encapsulated chemicals that on reaction dissolve their matrix is also conceivable, where a specific molecule, perhaps a tailored transmembrane protein, is used to suddenly lower the energy barrier keeping the compartments separate.

If nanomagnets could be configured that explode apart upon change of their configuration [42], this would allow another approach to TNB. The trigger could be a strong, short duration magnetic field. Biocompatible nanomagnets are available [43].

Other triggering mechanisms that could be considered include protective layer materials, passivation layer materials, and photoactivation.

In the spirit of bioinspiration [44], we find some more hints of how TNBs might be designed. For example, if a stiff tissue, say for a stent, were constructed of cells that could be triggered to undergo apoptosis [45] without affecting the rest of the body, then the disintegrating cells would be transported away by phagocytosis. Transient stiff embryonic tissues such as notochord [46] may provide a model. Differentiation waves through genetically modified tissues might cause those tissues to disintegrate to separate cells, such as

may occur in embryogenesis during neural crest formation [25b].

We will next review biological apparati that are triggered rapidly, sometimes explosively. We could envision nanosprings and nanoactuators inspired by the molecular spring (spasmoneme) in *Vorticella convallaria*:

“Molecular springs have recently emerged as the basis for the fastest and most powerful movements at the cellular level in biology. The spasmoneme of the protozoan, *Vorticella convallaria*, is a model molecular spring, relying on energy stored in protein interactions to power contraction over a few hundred micrometers in a few milliseconds. While basic characteristics of *Vorticella contraction* are known, the underlying biochemical mechanism is unclear” [47].

The speed of the spasmoneme is of the order of 0.1 m/s. Pollen also disperses explosively [48] at 3 m/s, and the jumping of some insects uses a trigger mechanism [49] to achieve 5 m/s. Spray from bombardier beetles [50] exits at up to 20 m/s. Exploding seeds of *Hura crepitans* [51] have initial velocities up to 70 m/s. Discobolocysts in the green alga *Ochromonas* [52] discharge at an estimated 300 m/s. Exploding ants [53] suggest the possibility of stents under pressure that disintegrate like burst balloons. We could use such fast actuators [54] to activate the destruction of stent material. The signal could be electrical and could be fed into the person *via* coils (as in cochlea implants [55]).

Resilin, the most stretchable natural rubber, can stretch twice its original length without breaking [56]. Chromolinkers, the material connecting chromosomes [57], can reportedly stretch 30x their relaxed length and return to their original length (Andrew J. Maniotis, personal communication). Cell colonies of the diatom *Ellerbeckia arenaria* grow many millimeters long and can be mechanically elongated three times their original length. When released, they snap back like a spring by an unknown mechanism [58], perhaps related to the elastic material between cells in another colonial

diatom, *Bacillaria paxillifer*, previously known as *B. paradoxa* [59].

Some organisms have motor proteins that exhibit signal-dependent length changes. Prestin, for example, is the motor protein in outer hair cells of the inner ear, the cochlea. Voltage applied to the prestin molecules results in length change. In the inner ear, this voltage comes from electrical signals via the auditory nerve from the brain. Voltage-induced shape changes can be elicited in cultured human kidney cells when prestin is expressed in them [60]. A material with prestin expressed in it might be of interest for use as stent material.

In general, we may classify TNBs as:

- 1 *metastable* in the implanted environment, so that the function of the trigger is to start the collapse to a stable, disintegrated state that propagates throughout the structure;
- 2 *stable* in the implanted environment, with the function of the trigger mechanism being to alter the components by changing them so the structure falls apart;
- 3 *logical*, i.e., separation on computer command of constituent nanobots.

Metastable structures are perhaps less desirable, because they can fall apart at an arbitrary time [61], before we get to trigger them deliberately.

In summary, there are many plausible materials for constructing Triggered, Nanostructured Biodegradables (TNBs).

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