Programmable Bio-Scaffolding: The Suture of the Future

Abstract

Every day, over two million people are forced to put their lives at risk by taking blood thinning medicines. People suffering from deep vein thrombosis, strokes, and diabetes all share the common fear of uncontrollable bleeding from open wounds. In the future, Programmable Bio-Scaffolding (PBS) system will eliminate this fear. PBS technology consists of DNA-coated hydrogel cubes, each containing a stem cell. The cubes represent pieces to a 3-D puzzle, sticking only to complementary cubes. PBS technology will accelerate the process by precisely scaffolding wounds through binding edges of the cut together with premade stem cells. PBS technology will enter the user's system intravenously or be applied externally to the wound. Patients could use PBS technology in concert with their blood thinning medication. By eliminating the fear of cuts and slow healing wounds, PBS technology is the suture of the future.

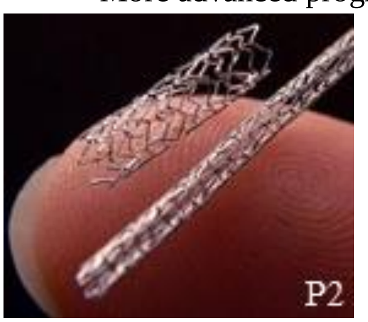
Programmable Bio-Scaffolding: The Suture of the Future

Present Technology

A programmable material is any material that has the ability to change its physical properties such as shape, conductivity, pH, surface tension, magnetic direction, or surface adhesion. A few known programmable materials include the following complex fluids, shape-changing materials, and self-assembling robots. These materials are all designed to have highly dynamic forms and functions.

Complex fluids are substances with the ability to change between two states. An example of a complex fluid is gallium. Gallium`s surface tension changes when different voltages and current are applied. Researchers use the phase change of gallium as a digital memory device. The solid and liquid interface represents the 1’s and 0’s of computer code.

More advanced programmable materials are **shape-changing materials** like memory wires. These materials have the ability to transform their shapes based on their temperature or voltage. One application of this material is a programmable stent used to open up blood vessels. Another application of this material is turning two-dimensional shapes into three-dimensional objects.



Robotics, AI, and claytronics could mimic the properties of programmable materials. One of the most successful is the Self-Assembling Kilobots designed by MIT and Harvard. Programmed to communicate, Kilobots are able to create specific shapes without individual commands. Researchers from both institutions have also created folding sheets. These sheets

can go from two-dimensional into three-dimensional by heating or cooling the fold marks on the sheets.

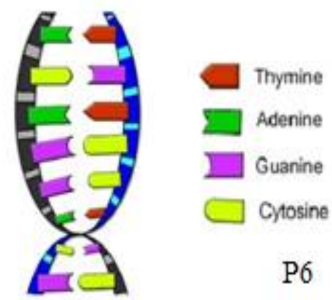
Our project relies on several advances in the medical field as well. Usage of **medical sutures** effectively closes an open wound but requires expertise from a trained doctor. During stitching, a doctor sews the two sides of the wound together so the body will have to scaffold less area, making the damage heal faster and reducing scarring.


P4

Another technology we built upon is **bioprinting**. This technology uses the patient's own cells, along with other bio-materials, to create a skin graft that fits to the patient's wound. Along with skin grafts, the machine can use the patient's cells to create other artificial organs.


P5

Programmable glue (PG) is a special material that joins the programmable material and biological technology. PG is made of DNA, and uses DNA's four-letter sequence as its code. A single strand of DNA binds tightly to a second one if they are completely complementary to each other. The application of PG could be demonstrated by dice (shown below). On a die, each side has a different number (DNA code), and only sides of dice with the same number stick together (finding matching parts). Researchers at the WYSS Institute, a joint lab of both MIT and Harvard scholars, have already used the PG to self-assemble 25 different hydrogel cubes into a specific shape consistently. The PG could have many varieties of binding codes because DNA can contain much information in only a short strand.



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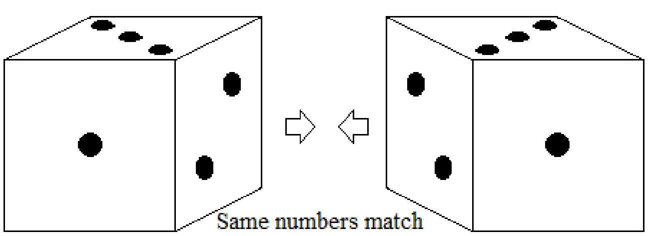


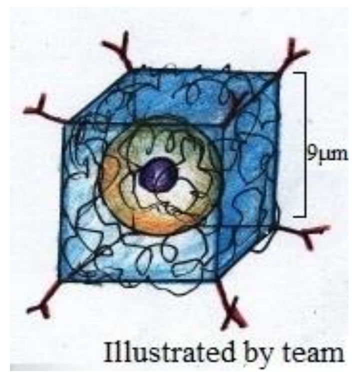
Illustrated by team

History

Although the idea of programmable matter hasn't been around long, the principles that it represents have existed for thousands of years. Ovid's epic, *Metamorphoses*, describes an ivory statue coming to life. Similarly, the Greek myth of Hephaestus is about a blacksmith who creates an automated bronze man named Talos. Even though today we are nowhere near creating autonomous, self-adapting, self-learning modular structures, many great strides have been made in search of perfecting the ultimate autonomous robot. In **1956**, Marvin Minsky, John McCarthy, Claude Shannon, and Nathan Rochester organized the Dartmouth Conference at which the field of AI was born. The birth of AI and its philosophy are based on the science of neural networking, which led Alan Turing to hypothesize that a computer could be shown to be capable of thought if it could carry on a conversation in what came to be known as Turing test. In **1987**, Toshio Fukuda created a cellular robotic system that could re-organize itself by rewriting its own software. In **1991**, the term "Programmable materials" was first coined in a paper by Toffoli and Margolus to describe computing elements that work to achieve a given task from fundamental bits of matter. In the early **1990s**, many papers came out on the theoretical problems of the implementation of self-configuring substructures; but despite the drawbacks, advancement in this new field continued. In **2007**, Skylar Tibbits founded SJET which prototyped materials that could transform between 2D and 3D figures. Dr. Michael Rubenstein, a professor at MIT, then created the Kilobot in **2012**. The idea of the Kilobot was that small identical individual robots could self-assemble to perform larger tasks as a group. In **2013,** Researchers at the WYSS Institute of Biology at Harvard created a biological rendition of this idea. They created cellular sized hydrogels that could self-assemble, similar to Kilobots.

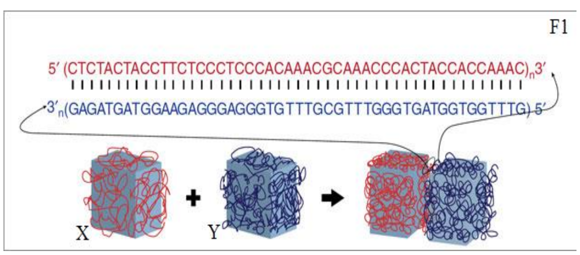
Future Technology

In the future, programmable glue will be used to make a highly efficient self-assembling scaffolding system to repair skin tissue. Normally when a person is cut, collagen, a connective protein, forms to create the foundation of the new tissue. This is a slow process that typically takes up to three weeks. Our Programmable Bio-Scaffolding (PBS) technology simulates this process to facilitate and promote fast healing of open wounds.

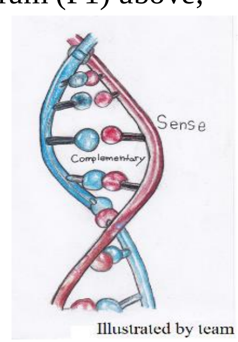


At its root, PBS is a technology that delivers specialized stem cells contained in hydrogels that stimulate the cell regeneration process. These hydrogel cubes are water-based substances containing sodium polyacrylate, which shelters the stem cells and promotes tissue regeneration. The six faces of the hydrogel cube are covered in "DNA glue," and four vertices of the cube have antibodies for sticking into skin cells.

Researchers from both Harvard and MIT have successfully designed similar biological

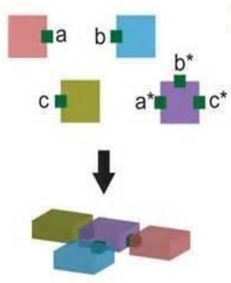


glue and have shown that it can self-assemble in a research lab. The programmable glue is made from multiple copies of a single DNA snippet combined into one strand of DNA, commonly referred to as the "giant DNA." In the diagram (F1) above,



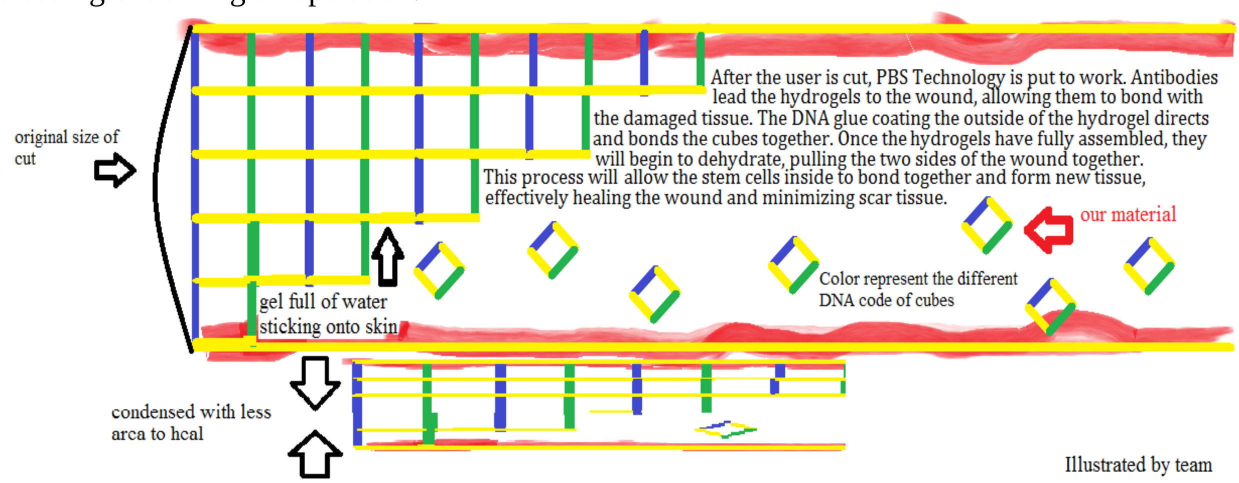
the two cube shaped materials are coated with two complementary senses (a single strand of the double-stranded DNA), X and Y. The senses coating the cubes act as the glue. Since the two strands are complementary, C matching with G, and T matching with A, the cubes X and Y would stick together when in proximity. However, if there is a difference between the two strands, then the two senses are not complementary and will not stick together. The coding of the glue is done by changing the nucleotides (C, G, T, and A). A single DNA strands can contain these chemical letters in

F2

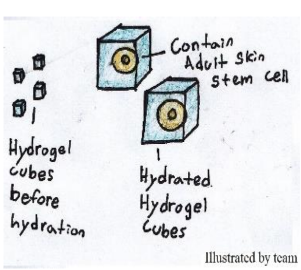


many different pattern, so there will be no risk of a repeated code. In the diagram (F2), using the programmable selective property, the cube would self-assemble into a specific shape due to the fact that the strand “a” could only stick to the “a*” complementary strand while “b” and “c” could only stick to their individual complementary strands as well. Because the DNA glue is programmable, it’s feasible to use this as a self-assembling technique to build an orderly scaffold to cover the cut, instead of a slow-forming jumbled mess of collagen fibers.

The goal of our PBS technology is to eliminate fear of uncontrollable bleeding in people who are at high risk such as those taking blood thinners for deep vein thrombosis, strokes, or diabetes. PBS technology also would allow for safer surgery because it would reduce the risk of bleeding out during an operation.

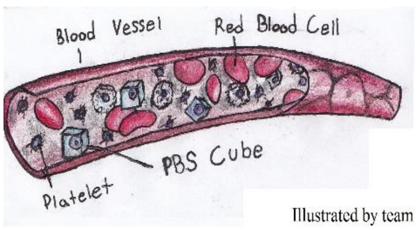


Shown in the diagram above, when the user gets a cut, corners (yellow) of the hydrogel cube that have the antibodies will attach to both sides of the cut. Other faces (blue and green)



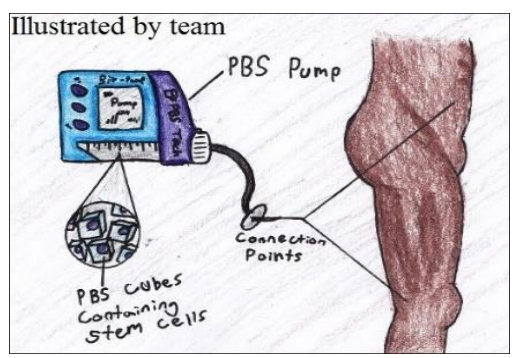
will each bound to complementary faces (matching colors), forming an artificial scaffold in a short amount of time. After the formation of the scaffold, the hydrogels will condense and get rid of the excess water that was used to moisturize the human cell that it was holding. Due to the condensing process of the hydrogel, the scaffold will decrease in area, thus pulling the two sides of the cut together. This process will allow the user's body to regenerate tissue for a much smaller surface area. With less surface area to regenerate and new cells already covering the damaged tissue, users will be able to heal the wounds significantly faster than normal. The actual speed of the healing process will still depend on the user and a few different variables such as age, damage, and the environment.

While the glue is only able to stick to what we programmed, there must be a way for our regenerative material to stay in the human body without the risk of being eliminated by white



blood cells. Recent study on human immune systems suggests that it is possible to bypass the human immune system when non-native materials are attached to a native material in the human body. In our product, each block of hydrogel would be attached to a universal protein that is viewed as native by nearly every immune system. The regenerative materials would float through the human body freely without any mistaken intervention from the immune system.

The materials would enter the cut externally through a PBS patch or intravenously through a PBS pump. The pump is very precise and efficient because it would be directly transferred into the bloodstream. The goal of this system would be to lessen the demand for one-on-one medical care while not creating additional problems for the user. The Band-Aid like system is another method of administration. It is simple and safe, with the needed materials already on the patch. It makes the transportation of the hydrogel cubes simple because it would be administered directly to the wound. The main drawback to the patch would be that it only works when attached to the body.



Breakthroughs

In order for our Programmable Bio-Scaffolding (PBS) material to work, five breakthroughs are needed.

Breakthrough #1: Fabrication

Our technology needs to be small enough to flow freely in the bloodstream—a red blood cell is typically only 6 to 8 micrometers in length. Making a mechanical system that could manufacture something so small and detailed is a technical feat, and is one of the biggest setbacks to creating PBS on a large-scale.

Manufacturing synthetic DNA to cover the hydrogel and give it its programmable properties also presents challenges. Although researchers have recently discovered that it is possible to create synthetic DNA, its production is still a slow and new process. Similarly, the antibodies that are needed to attach directly to the skin cells have not been developed. These manufacturing breakthroughs are needed before PBS's programmable glue can be fully functional.

Breakthrough #2: Method of Application

The PBS patch would require a medical adhesion that could release PBS technology when applied to the wound. The bandage would also need to consist of storage for the PBS technology and a timer to release it. Along with that, the patch must have the ability to be reloaded with the PBS technology because the stem cells that it contains are user specific. Alternatively, a PBS pump could be used to transfer the technology into the bloodstream. Much like the PBS patch, the PBS pump would need a storage area and a timer. It would also need a way to access the bloodstream such as a catheter.

Breakthrough #3: Anti-rejection

Our PBS technology needs to flow freely in the human bloodstream to find cuts or damage. The immune system would need to ignore PBS materials or mark them as native so our material would be able to survive in the human body for long periods of time. Researchers of viruses and immune system have suggested that it would be possible to do so by attaching the materials to a protein, but as with most systems, further researches will be needed.

Breakthrough #4: Reactive hydrogel

In our PBS system, we use hydrogel as a healing device as well as a transportation device. Normally, for a large cut, the edges must be pulled together to promote fast healing. This is usually done by using sutures. The hydrogels must not only be able to provide scaffolding for the new stem cells, but also be dynamic in their shapes. By "shrinking," the wound will effectively be pulled together. Before this can happen, bio-engineers must design a reactive hydrogel that can change its surface area based on chemicals released by the body that indicate injury. One example would be to pick up on pH levels in the blood. When this is done, the hydrogel would be able to effectively act as a suture as well as a bio-scaffold.

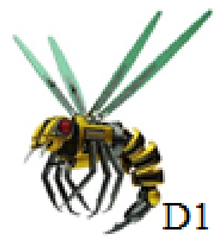
Breakthrough #5: Universal stem cell

Every human has different skin cells. In order to mass produce the PBS material, we would need to find a universal stem cell that we can use on everyone. Currently, there is already much research and testing on universal cells, especially blood cells. This breakthrough should be reality in the very near future.

Design process

Originally, we were working on swarm technology in our honors research class. Our group found inspiration through the idea of self-assembling robots. When our teacher approached us about this competition, we knew we wanted to do something along the lines of autonomous computing. Before electing to pursue the PBS technology, we had several other ideas involving autonomous self-assembling systems.

The idea that we started out with utilized self-assembly of robots. These robots would be individuals that did not have an abundance of capability as a lone unit but would be able to self-assemble as a collection of robots and would have the capability to complete larger and more significant tasks. Self-assembling robots would be particularly useful in space. We thought we could drop individual, identical robots that could swarm and build space shuttles. We thought we could mimic bees; while individual bees do not have many abilities on their own, they self-assemble to form a working society. Through this action, bees can perform larger tasks. Although a great idea for the future, we chose not to pursue this project because we thought we could find a better use for self-assembling systems.



D1

A second idea included the use of programmable materials to construct an "All-in-One Tool Kit." This idea eliminated the necessity of buying different tools for different jobs. The science community has recently discovered and made many advances in the field of programmable materials and is brainstorming different applications for these materials. An "All-in-One Tool Kit" would include memory-wire-like materials that could be transformed into different tools or household applications. This would allow the user to utilize a single material to complete a variety of jobs. One of the places this "All-in-One Tool Kit" could be particularly useful today would be in space. If people learned anything from the Apollo 13 launch, it's that crisis management relies on creativity and versatility. Although the "Utility/All-in One Tool Kit" might have an impact in many areas, we chose not to pursue it because we ultimately decided we wanted to focus our efforts on technology that would be used on Earth as opposed to on the Moon or Mars. We also realized that this versatility would be crucial in the medical field as well.

Surgeries could be revolutionized if specialized tools could be changed to best fit the surgery requirements. From this we found the interest to pursue a topic in medical field. It was very important to us (although not all of us knew it at the time) to help people by doing a project that has to do with modern medicine.

A third idea came to us after we read a paper about programmable glue. Scientists were developing programmable glue in their laboratory (and then interviewed the author via Skype). We were very interested in this idea, but we wanted to go one step further in its medical application. What if these hydrogels, these magical healing-all substances, could be constantly in the human the body? After we pondered that idea for a while, we came up with a grand solution: a pill that uses these glue-wrapped hydrogels to transport stem cells around the body. Once they found the damage, they could arrange themselves to fit the wound and then start to re-heal the damaged area. As we were developing this idea, we learned we needed to modify the idea because this technology could not be taken in the form of a pill. Unfortunately, the hydrogels couldn't physically be absorbed by the body because they are too big to pass through the small intestine wall. Our interest focused on our final design when we realized that programmable glue could be used to heal wounds when applied externally or through direct infusion into the blood stream.

Consequences

Every action will have a reaction. The PBS technology causes a change in people's thinking, which can create positive or negative consequences.

(−) PBS technology may be controversial because it involves putting artificial technology in the human body, a practice some people disapprove.

(−) PBS technology contains stem cells, about which many religions have reservations. However, this controversy has been diminished slightly with advancements in biological technology.

(−) The process to make PBS technology is currently unknown, but it is reasonable to believe that initial costs for the user will be very high, as are all new medical advances.

(−) Initial imperfections in early versions could be prone to failure leading to the clogging of veins.

(+) With our PBS system, human can speed up the healing process and shorten recovery time.

(+) With fast healing times, people on blood thinners can live free of the fear of cuts.

(+) By protecting people from uncontrollable bleeding, PBS ensures the user a more normal life and confidence in their preferred lifestyle.

(+) PBS technology is entirely autonomous and does not require doctor supervision. This feature makes it very convenient to use.

(+) PBS can be applied through patches or pumps, making it a very versatile medical technology.

(+) People on blood thinners can be operated on without the fear of uncontrollable bleeding.

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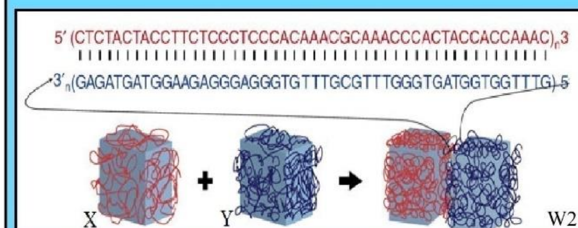
Explore the Future

The Problem:

People who use blood thinning medicines or have been diagnosed with blood thinning diseases suffer from uncontrollable bleeding.

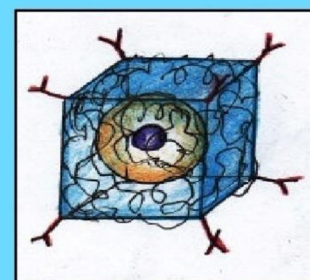
Explore:

Learn more about how hydrogel and programmable glue combine to create the exciting future of Programmable Bio-Scaffolding.



The Solution:

The problem is clear; the solution is simple. See how our project is going to change the world.



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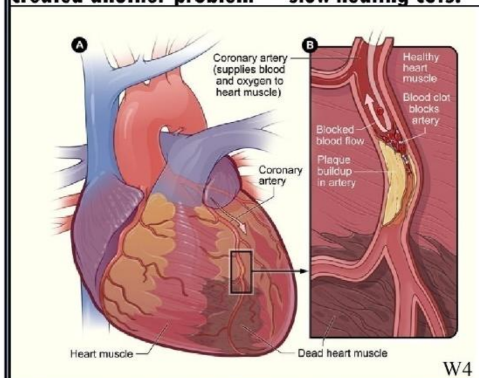
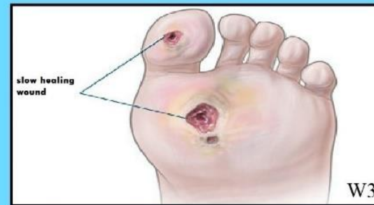
Explore the Future

Problems Today:

Blood thinners or anticoagulant are drugs that prevent clotting of blood. They are crucial in treating diseases like stroke, heart attack, and deep vein thrombosis. Although drugs like Warfarin fix the problem of clotting, they also created another problem— slow healing cuts.

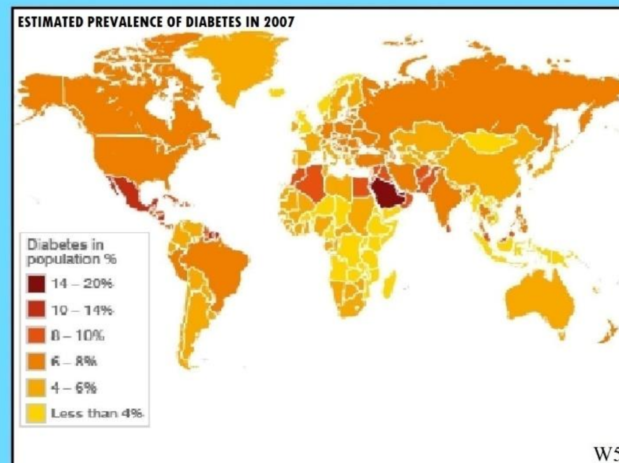


W4



W3

Small wounds could end up like the picture above if not treated.



W5

There are over two million people taking blood thinners every day, and much more are effected by blood thinning diseases like diabetes.

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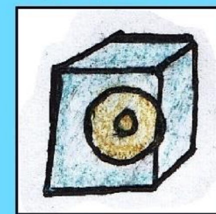
PBS Design:

Tissue Stem Cell:

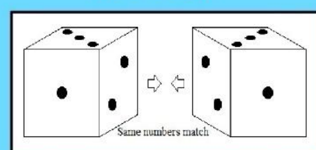
- Each cube contains a single stem cell compatible with the host body, in order to speed up the healing and tissue regeneration process.

Hydrogel Cube:



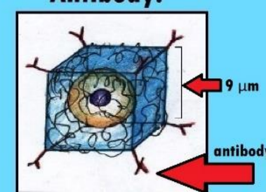
- The cells are contained in a cube of hydrogel, that shrinks and dissolves in order to pull the two sides of the wound together.

DNA Glue:



- DNA is made up of two complementary strands, which bond with each other. Each hydrogel cube is wrapped in one of these complementary strands, allowing the cubes to "glue" together.

Antibody:



- On each vertex of the cube is an antibody, allowing the PBS system to latch on to the edge of the wound and surounding tissue.

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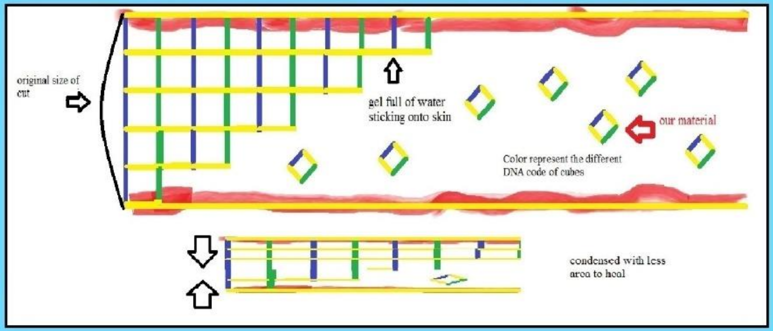
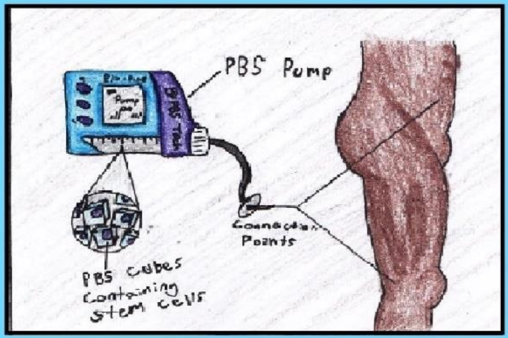
Our Product:

Scaffolding:

After the user is cut, PBS Technology is put to work. Antibodies lead the hydrogels to the wound, allowing them to bond with the damaged tissue. The DNA glue coating the outside of the hydrogel directs and bonds the cubes together. Once the hydrogels have fully assembled, they will begin to dehydrate, pulling the two sides of the wound together. This process will allow the stem cells inside to bond together and form new tissue, effectively healing the wound and minimizing scar tissue.





PBS Pump:

Our PBS Pump is similar to modern insulin pumps, but rather than injecting fluid directly under the skin of the abdominal cavity, our pump uses a stent. This stent allows PBS material to flow directly into the user's blood stream. The pump itself completely regulates the flow of our product, and displays information regarding dosage and remaining material.

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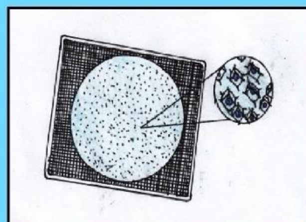
The Future:

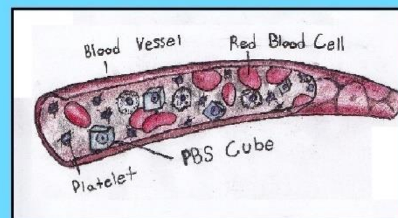
For too long, people on blood thinning medications have had to worry about their every move. Even a small cut could lead to severe probems, but with our PBS technology that will no longer be the case. And the benefits of this technology don't stop there.

The PBS Patch:



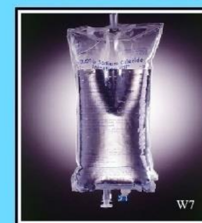
The PBS Patch is coated in a layer of PBS hydrogel cubes, making it perfect to slow bleeding of surface wounds on the spot.

In The Bloodstream:



PBS Technology is fully capable of existing in the user's bloodstream to take immediate action in case of a cut, allowing the user new peace of mind.

Surgery Recovery:



Recovery from surgery can often be a long process. But with the introduction of PBS technology into the bloodstream or externally on the patient, recovery times could be significantly cut down, and scarring reduced.

This and more means Programmable Bio-Scaffolding Technology truly is...

The Suture of the Future.

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