Self-assembling Nanotube-based Circuits with Collagen Substrates

Sharlene Coleman  David Elihu  Sarah Frost
Mills College  Massachusetts Institute of Technology  University of Notre Dame
Todd Hoffenberg  Ziyad Jabaji  David Karig
Georgia Institute of Technology  Stanford University  Princeton University
Elena Losseva  Don Riggs
University of Western Ontario  Union College

Abstract

We suggest several assembly strategies for creating a collagen substrate capable of supporting a self-assembling carbon nanotube based circuit. Several strategies are explored and their strengths and weaknesses highlighted. A novel structure consisting of yeast-generated flat collagen strands with ‘sticky ends’ which tile to form a flat lattice structure is proposed as the support for a carbon nanotube circuit. The nanotubes are affixed to the collagen base by a double-sided molecule consisting of a pyrenoid moiety that binds carbon nanotubes and an antibody-functional tail that binds to collagen.

1 Collagen Introduction

Collagen, the most abundant protein in the body, provides structure and resilience to tissues. Collagen has a right-handed triple helical framework, and its composition is characterized by an abundance of two amino acids, glycine and proline. Glycine is essential for the right-handed triple helix structure, and collagen is typically composed of a three amino acid chain that consists of glycine and two other amino acids. Collagen’s rigid yet flexible structure makes it a suitable construction material. The ability to choose from the 20 amino acids in the other two amino acid chains of the structure gives additional flexibility in designing specific collagen strands. Similarity to nanotubes in size is another factor in favor of using collagen as a building material for nanocircuits. A typical collagen molecule is 300 nm long and 1.5 nm in diameter, quite similar to the 1.1 nm diameter of a carbon nanotube. Another major advantage of using collagen in the molecular framework is its strength, which is due to the hydrogen bonds chaining the triple helix together. Researchers have recently reported electrospinning of collagen nanofibers and in-vitro development of collagen.

2 Nanotube Introduction

Carbon nanotubes are single cylindrical molecules in the fullerene molecular family that exhibit the same closed structure as buckyballs; nanotubes extend into long strands rather than forming a spherical structure. Nanotubes are extremely resistant to stress. They form as single walled nanotubes (SWNT) or multiwalled nanotubes (MWNT). Both SWNT and MWNT share the exciting electrical properties which make them attractive for use in nanoelectronics. The single walled nanotubes are considered here due to their smaller size and simpler structure.

There are three types of nanotubes that differ in the angle at which they are rolled. Depending on this angle, nanotubes can function either as semiconductors or conductors. The types include armchair, zigzag, and chiral. The 'armchair' type exhibits metallic conductivity and resistance that increases with heat [5][19]. The chiral type produces semiconducting nanotubes. The architecture considered later in this paper requires both metallic and semiconducting nanotubes. There are several known production methods such as chemical vapor deposition[7] and arc discharge[12] among others [10]. However, there is no known method for grow-
3 Collagen Assembly Strategies

3.1 Overlap Strategies

The construction of a self-assembling carbon nanotube lattice with a collagen substrate naturally begins with substrate assembly. In nature, collagen triple helix strands bond together in parallel rows, head to tail, with a gap between the head of one and the tail of the next and an offset between the parallel rows.

With this structure in mind, several design strategies were considered. The first and most obvious was to construct a grid of single collagen strands (see figure 1). The obvious defects in this model are the limited binding surface available where the two strands meet at a 90 degree angle and the existence of gaps between the head of one strand and the tail of the next. Creating a good bond with this structure is problematic because the diameter of a single collagen strand is 1.1 nm, providing a limited surface area for bonding.

A second strategy seeks to take advantage of the offset when parallel collagen strands bond to one another. See figure 2. In this strategy, junctions present at the parallel fiber overlaps would contribute significantly to the strength of the resulting structure by providing multiple points of contact for the perpendicular strands, and the presence of multiple strands eliminates the potential problem of gaps between the head of one fiber and the tail of the next. Two types of collagen strands would be required, one with suitable binding sites for nanotubes and the other without (figure 3).

This strategy can be scaled up to include multiple strands with proportionally greater contact area, perhaps with alternating types of collagen strands (figure 4).

Collagen strands designed to form a single 90 degree bend might lend themselves to an assembly strategy using tiling (figure 6).

One of the ways to construct regular grids out of collagen is to join collagen triple helices to form the vertices of a grid. Several grid types can be envisioned, depending upon how many helices can be joined in a knot (figure 7). Note that it is not possible to join 3 helices, since the number of individual strands to be joined is odd. It is possible, however, to design a tile containing a node of 4 collagen helices, which, if assembled into a sheet would form a regular grid.
The design of a tile is governed by two major factors: strand orientation within each helix must coincide and it should be possible to arrange tiles side by side as to cover the plane. The first of the following tiles (figure 8) has the problem that the three sequences in each helix do not have the same orientation. The second tile cannot be used either because the direction of the helices do not allow for sequential tiling. The last of these tiles permits the construction of a grid as shown in figure 3.1. Note that the junction needs to be flat in order to avoid rigidity problems.

As an aside, one might reasonably question whether this structure already exists in nature. If it could be constructed in vitro, a binding antibody could be found and employed to search for the identical structure in vivo.

The first step in the self-assembly of the collagen grid is to engineer the strands needed to form a tile. Yeast cells have demonstrated the expression of collagen. Using bacterial culture for the manufacturing of collagen would be optimal because of the possible simplicity of the cell which would al-
low better control over the production process. Current DNA production techniques must be extended for specifically engineering collagen. Care must be taken to ensure that there is a unique way for the engineered strands to bind to each other (six are required). This can be achieved by using appropriate amino acids to differentiate all binding sites. In order to construct the collagen lattice, the utilization of a seed tile as well as edge tiles will be required. As in DNA-tiled structures, an assembled sheet may be prone to errors involving tiles twisting and binding incorrectly if tiles are not sufficiently rigid (for discussion of tiling see for instance [17][9]). A reinforcing mechanism may be necessary to provide additional rigidity.

3.2 Molecular Lashing

Molecular lashing, utilizing a molecule such as rotaxane to attach to and reinforce the juncture, is an example of such an approach. Such a scheme involves searching for molecules that could bring about binding equivalent to rope lashing. The molecule pictured in figure 11 is a didactic example that demonstrates the likely nature of the four "arms" desired for reinforcing a four-way collagen junction, in which two such molecules come together and fuse over the collagen intersection.

![Figure 11. Conventional (diagonal) rope lashing and a molecule that could (theoretically) do the equivalent when two come together and react over the intersection.](image)

4 Glues

4.1 Antibodies

Various possibilities exist for attaching nanotubes to collagen. Antibodies, which are “Y-shaped” immunoglobulins that bond to epitope sites on antigens, are a useful tool. An epitope site is a sequence of typically six or fewer amino acids. Bonding between antibodies and antigens is non-covalent [13]. Figure 12 shows a typical antibody, which consists of two heavy chains and two light chains. The variable region is the portion of the antibody that binds to the antigen. Recall that proteins can be conjugated to antibodies and that secondary antibodies can bind to the constant regions of other antibodies.

![Figure 12. Typical antibody](image)

In order to avoid interfering with the electrical properties of the nanotubes, no covalent bonds may come in contact with them. A team at Stanford presents a non-covalent method for immobilizing biomolecules on the surfaces of carbon nanotubes [4]. This method creates several options for attaching nanotubes to collagen, and since the bonds between antibodies and antigens are non-covalent, antibodies could also be directly attached to nanotubes without affecting their behavior. Two examples have been shown in Figure 13 to illustrate possibilities for attaching nanotubes to collagen. In the first example, the method presented in [4] would be used to immobilize streptavidin on the surface of nanotubes. Streptavidin is a tetramer capable of irreversibly binding biotin molecules. Thus, a biotin conjugated antibody that binds to collagen can be used to link collagen to the streptavidin on the nanotube. In the second example, ferritin is immobilized on the nanotube surface. A protein having both a binding site for ferritin and a binding site for collagen could be engineered, possibly by linking two antibodies, to attach the nanotube to the tile. Other options are available [8][16][20][18].

4.2 Nanotube Functionalization

We must address the question of how to functionalize – and hence bind, manipulate, and assemble – nanotube molecular wires. The problem at hand is not to be considered within the paradigm of traditional chemical functionalization, as we have to be exceedingly careful not to disrupt the delocalized electronic system in each nanotube molecule. One extremely attractive solution consists of employing the molecule pictured in figure 14, with delocalized aromatic groups that can bind non-covalently and irreversibly to nanotubes, providing an ideal ligand that can easily be attached to collagen substrates through traditional chemical synthesis.
and reactivity.

Figure 14. Structure of the ligand (1-Pyrenebutanoic Acid, Succinimidy l Ester) used by the Dai group at Stanford in order to functionalize nanotubes and anchor proteins[4].

5 Architecture

From the standpoint of building useful circuits out of the established molecular toolkit, the circuit architecture becomes very limited. Only single-walled nanotube (SWNT) intersections will be considered. Charles Lieber (et al.) has demonstrated a termed electrostatic switch using nanotubes, which requires nothing more than a SWNT cross-point. If placed with lithography techniques, the nanotubes will separate in the z-dimension to approach a mechanical minimum. The resistance between these nanotubes is finite and very large. However, if the nanotubes are held at opposite electrical polarities, they can be effectively doped in a non-volatile but still reversible manner. This will cause the nanotubes to attract, and the z-dimension distance between them will be held at a van der Walls minimum (ON state). The resistance here is still finite, but it is orders of magnitude less than the mechanical minimum (OFF state). Both switch states are shown in Figure 15.

The resistance difference between states spans 5 orders of magnitude. It is important to note that this device can be made with any combination of semiconducting and metallic nanotubes; however, implanting diode characteristic (essential for wired logic) into an intersection requires a lower layer of semiconducting wires (not necessarily nanotubes) and an upper layer of metallic nanotubes [11] [14]. Unfortunately, there is no current way of separating semiconducting from metallic nanotubes, but it must be presumed this will soon be possible. To construct a RAM, which could be done at present, a crossbar grid is most convenient. To be defect tolerant, a good addressing scheme must be considered. On a nano-scale, work done by Phil Kuekes HP Labs and separately by Andre DeHon [6] proposes solutions to addressing large crossbar architectures. More importantly, this applies to logic. If a 5 nm separation between parallel nanotubes is achieved, informational density is comparable to $10^{12}/cm^2$, and switch speed can approach 200 GHz [11]. For large-scale crossbar logic architecture and a demonstration of fault tolerance, the Teramac can be considered a reference point [15]. Because the scaffolding is not intolerant to heat, power dissipation must be considered. If each device operates as Lieber outlines, a 0.3V supply and 3 microA current per device is reasonable [11]. Applying this to one device at each row continually operating at one time, the overall power consumption is near 3W, which may eventually become significant. Additionally, this architecture is susceptible to transient failure from radiation or, potentially, other external effects. Error correction and detection may be difficult to accomplish because the structure is intentionally left as simple as possi-
ble for tiling reasons. It should also be noted that the stress on a nanotubes in the ON state is within bounds, but additional stress in the tiled product may become a factor.

6 Other

6.1 Final Assembly

The creation of a collagen lattice and a method of attaching carbon nanotubes to the collagen structure has been presented. The final step involves positioning a second layer of nanotubes, perpendicular to the first, to form a crossbar architecture.

These layers are combined so the two nanotube layers are both inside the collagen layers which would be secured together with a molecule that bonded to each of the collagen lattices. This molecule would need to be designed carefully to control the distance between the nanotube layers. The two layers need to be near enough to allow the formation of switches at the nodes.

6.2 Future Possibilities

Recall why collagen has been suggested as a material for the nanotube support structure. Precise collagen strands can be manufactured by cells, and the resulting structures will be quite rigid and strong. The collagen used in this lattice will be carefully engineered. Knowledge of the makeup of collagen and the form which it should ultimately take, i.e. a lattice, along with mechanisms available in nature for repairing and replacing collagen can be exploited. Since it is known what the structure should be, a mechanism can be designed to recognize faults in this structure and mark them for replacement or repair. Since the collagen will be on the outside of the nanotube “sandwich,” perhaps organisms can be created that will actively seek out these collagen lattice faults. While faults and errors are expected in a self-assembled structure, the existence of an active fault detection and correction mechanism may decrease the number of permanent faults and increase the overall lifetime of a system by repairing the lattice when it begins to succumb to natural predators in the environment such as stray particles and unwanted chemical reactions. This self-repairing property will demand a more versatile architecture adapted to these intermittent faults.

7 Acknowledgement

The authors would like to extend a special thanks to Tom Knight for the initial inspiration and generously spending several hours discussing ideas and possibilities.

References


