

Programmable Assembly at the Molecular Scale: Self-Assembly of DNA Lattices (Invited Paper*)

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Abstract

DNA self-assembly is a methodology for the construction of molecular scale structures. In this method, artificially synthesized single stranded DNA self-assemble into DNA crossover molecules (tiles). These DNA tiles have sticky ends that preferentially match the sticky ends of certain other DNA tiles, facilitating the further assembly into tiling lattices. DNA self-assembly can, using only a small number of component tiles, provide arbitrarily complex assemblies. The self-assembly of large 2D lattices consisting of up to thousands of tiles have been recently demonstrated, and 3D DNA lattices may soon be feasible to construct. We describe various novel DNA tiles with properties that facilitate self-assembly and their visualization by imaging devices such as atomic force microscope. We discuss key theoretical and practical challenges of DNA self-assembly, as well as numerous potential applications. We briefly discuss the ongoing development of attachment chemistry from DNA lattices to various types of molecules, and consider application of DNA lattices (assuming the development of such appropriate attachment chemistry from DNA lattices to these objects) as a substrate for: (a) molecular robotics; for manipulation of molecules using molecular motor devices, (b) layout of molecular electronic circuit components, (c) surface chemistry, for example ultra compact annealing arrays. We also discuss bounds on the speed and error rates of the various types of self-assembly reactions, as well as methods that may minimize errors in self-assembly.

1 Introduction to Tiling Self-Assemblies

1.1 Self-Assembly: This is a process involving the spontaneous self-ordering of substructures into superstructures.

Biological Self-Assembly. We take inspiration from the cell, which performs a multiplicity of self-assembly tasks, including the self-assembly of cell walls (via lipids), of microtubules, etc. Many of these biological self-assembly processes

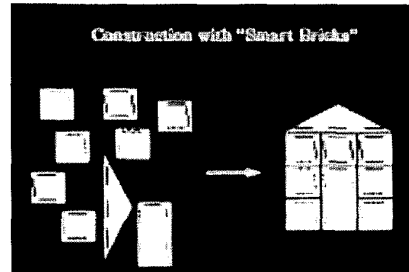


Figure 1: A tiling assembly using ‘Smart Bricks’ with affinity between colored pads.

utilize the specificity of ligand affinities to direct the self-assembly. We will focus instead on self-assemblies whose components are artificially constructed tiles.

1.2 Domino Tiling: These were defined by Wang [Wang61] (Also see the text [Grunbaum, et al, 87]). The input is a finite set of unit size square tiles, each of whose sides are labeled with symbols over a finite alphabet (the pads). Additional restrictions may include the initial placement of a subset of these tiles, and the dimensions of the region where tiles must be placed. Assuming arbitrarily large supply of each tile, the problem is to place the tiles, without rotation (a criterion that cannot apply to physical tiles), to completely fill the given region so that each pair of abutting tiles have identical symbols on their contacting sides. (See Figure 1.)

Domino tiling problems over an infinite domain with only a constant number of tiles was first proved by [Berger66] to be undecidable; proofs rely on constructions wherein tiling patterns simulate single-tape Turing Machines (see also [Berger66, Robinson71, Wang75]). Other results include reductions of NP-complete problems to finite-size tiling problems [LewisPapa81, Moore00]

1.3 Self-Assembly of Tiling Lattices. Domino tiling problems do not presume or require a specific process for tiling. However, we will presume the use of the self-assembly processes for construction of tiling lattices. In this self-assembly process, the preferential matching of tile sides facilitates the further assembly into tiling lattices. The sides of the tiles are assumed to have some methodology for selective affinity, which we call *pads*. Pads function as programmable binding domains, which hold together the tiles.

Since domino tiling problems are undecidable (see Section 3), tiling self-assemblies can theoretically provide arbitrarily complex assemblies even with a constant number of distinct tile types. As a very simple example, it is possible to construct tiling assemblies with self-delimiting boundaries (e.g., rectangular boundaries of a given width w and length h), by use of a set of wh distinct tiles, with w distinct pads types on the bottom and top of a set of square tiles and a set of h pad types on the other sides of these tiles, and this can also be done with a constant number of distinct tiles. (See [Rothemund and Winfree, 2000b] for improved program-size complexity of self-assembled squares.)

Pad binding mechanisms for the preferential matching of

*A postscript version of this paper is at URL <http://www.cs.duke.edu/~reif/paper/SELFASSEMBLE/nanoassemble.ps>

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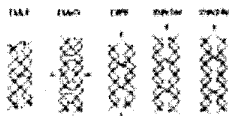


Figure 2: Double crossover isomers. tile sides can be provided by various methods:

- (i) *molecular affinity*, using for example hydrogen bonding of complementary DNA or RNA bases,
- (ii) *magnetic attraction*, e.g., pads with magnetic orientations constructed by curing the polymer/ferrite composites in the presence of strong magnet fields, and also pads with patterned strips of magnetic orientations,
- (iii) *capillary force*, using hydrophobic/hydrophilic (capillary) effects at surface boundaries that generate lateral forces,
- (iv) *shape complementarity* (or conformational affinity), using the shape of the tile sides to hold them together.

There are a variety of distinct materials for tiles, at a variety of scales:

(a) **Meso-Scale Tiling Assemblies** have tiles of size a few millimeters up to a few centimeters. Whitesides at Harvard University has developed and tested multiple technologies [Zhao, et al, 98] [Xia et al, 98a,98b], [Bowden, et al 98], [Harder, et al 00] for meso-scale self-assembly, using capillary forces, shape complementarity, and magnetic forces (see <http://www-chem.harvard.edu/GeorgeWhitesides.html>). [Rothemund, 2000] also gave some meso-scale tiling assemblies using polymer tiles on fluid boundaries with pads that use hydrophobic/hydrophilic forces. A materials science group at the U. of Wisconsin also tested meso-scale self-assembly using magnetic tiles (<http://mrsec.wisc.edu/edetc/selfassembly>). These meso-scale tiling assemblies were demonstrated by a number of methods, including placement of tiles on a liquid surface interface (e.g., at the interface between two liquids of distinct density or on the surface of an air/liquid interface).

(b) **Molecular-Scale Tiling Assemblies** have tiles of size up to a few hundred Angstroms. Specifically, DNA tiles will be the focus of our discussions in the following sections.

1.4 Goals and Organization of this Paper. The goal of this paper is describe techniques for self-assembly of DNA tiling arrays and applications of this technology. We give in Section 2 a description of self-assembly techniques for DNA tilings and discuss the kinetics of self-assemblies and error control in Section 3. We discuss applications in Section 4. Section 5 concludes the paper.

2 DNA Self-Assembly of DNA Tilings

2.1 DNA as a Construction Material. Nano-fabrication of structures in DNA was pioneered by the Seeman laboratory ([Seeman82, 94b, 96a]), who built a multitude of DNA nano-structures using DNA branched junctions [Seeman89, Wang91a, Du92]. These previous systems were flexible, so control over synthesis and proof of synthesis were both limited to the topological level, rather than the geometrical level (in contrast to the tiles described below). These DNA nano-structures included: DNA knots [Seeman93], Borromean rings [Mao97], a cube [Chen91], and a truncated octahedron [Zhang94] (reviewed in e.g. [Seeman98] [Seeman94b] and [Seeman96a]).

2.2 DNA Tiles Constructed from DX and TX Complexes. The building blocks in the tiling constructions to be discussed are branched DNA complexes,

which we call *DNA tiles*, consisting of several individual DNA oligonucleotides that associate with well-defined secondary and tertiary structure (see [Winfree, et al 98] and below description of DX and TX tiles). These associate with well-defined secondary and tertiary geometric structure (which is much more predictable and less flexible than DNA nano-structures using DNA branched junctions). These complexes come in a number of varieties that differ from one another in the geometry of strand exchange and the topology of the strand paths through the tile. The branched DNA complexes used for tiling assemblies include the double-crossover (DX) and triple-crossover (TX) complexes, The DX and TX complexes consists of two (three, respectively) double-helices fused by exchange (crossover) of oligonucleotide strands at a number of separate crossover points. Anti-parallel crossovers cause a reversal in direction of strand propagation through the tile following exchange of strand to a new helix. For example, DAO and DAE are double-crossover DX tiles with two anti-parallel crossovers¹. (See Figure 2.)

DX complexes have been used successfully as substrates for enzymatic reactions including cleavage and ligation [Liu, Sha and Seeman,99]. The TX (see [LaBean,99]) TAO and TAE tiles, are similar except that they have three double-helices interlocked by exchange of oligonucleotide strands at four separate crossover points, two between the first pair of helices, two between the second (See the TAO in Figure 3 and the TAE in Figure 4. Both DX and TX motifs are useful for tiling assemblies; the DX (TX) complexes provide up to four (six, respectively) ssDNA pads [Liu, et al 99a] for encoding associations with neighboring tiles.

2.3 DNA Tiling Lattices. Tile assemblies, or simply tilings, can be defined as superstructures or lattices built up from smaller, possibly repetitive, component structures. Individual tiles interact by annealing with other specific tiles via their ssDNA pads to self-assemble into desired superstructures. These lattices can be either: (a) *non-computational*, containing a fairly small number of distinct tile types in a repetitive, periodic pattern; or (b) *computational*, containing a larger number of tile types with more complicated association rules which perform a computation during lattice assembly.

¹The structure of the TAE resembles the TAO in that it is constructed of three double-helices linked by strand exchange, however, it contains an Even (rather than Odd) number of helical half-turns between crossover points. Even spacing of crossovers allows reporter strands (shown in black) to stretch straight through each helix from one side of the tile to the other. These three horizontal reporter segments are used for building up a long strand which records inputs and outputs for the entire assembly computations. A 3D confirmation of the TAE tile has been rendered by Brendon Murphy at Duke University; see <http://www.duke.edu/~bkm2/taehtml/present.html>.



Figure 3: The TAO tile and a Strand and Sequence Trace through the TAO Tile.

DNA tiles are designed to contain several short sections of unpaired, single-strand DNA (ssDNA) extending from the ends of selected helices (often called 'sticky ends') that function as programmable binding domains, which are the *tile pads*.



Figure 4: The TAE Tile.

These DNA self-assembly procedures generally will be described as occurring in two distinct stages:

- (i) annealing of ssDNA into tiles; and
- (ii) assembly of tiles into superstructures.

However, direct assembly of DNA lattices from component ssDNA is also possible, and has in fact already been demonstrated for non-computational DNA lattices described below.

Programming Self-Assembly of DNA Tilings.

Programming DNA self-assembly of tilings amounts to the design of the pads of the DNA tiles (recall these are sticky ends of ssDNA that function as programmable binding domains, and that individual tiles interact by annealing with other specific tiles via their ssDNA pads to self-assemble into desired superstructures). The use of pads with complementary base sequences allows the neighbor relations of tiles in the final assembly to be intimately controlled; thus the only large-scale superstructures formed during assembly are those that encode valid mappings of input to output. The papers [R97, WLW+98, WYS96, LYK+00, LWR99, RLS00, MLR+00] describe methods for executing computation using DNA Tilings (due to length limitations in this paper, we have omitted a detailed discussion of DNA computational tilings).

The Speed of Computing via DNA Tiling Assemblies (compared with silicon-based computing.

The speed of DNA tiling assemblies is limited by the annealing time, which can be many minutes, and can be 10^{11} slower than a conventional computer. A DNA computation via self-assembly must take into account the fact that the time to execute an assembly can range from a few minutes up to hours. Therefore, a reasonable assessment of the power of DNA computation must take into account both the speed of operation as well as the degree of massive parallelism. Nevertheless, the massive parallelism (both within assemblies and also via the parallel construction of distinct assemblies) possibly ranging from 10^{15} to 10^{18} provides a potential that may be advantageous for classes of computational problems that can be

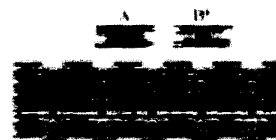


Figure 5: AB* Array. Lattice formed from two varieties of DX, one containing an extra loop of DNA projecting out of the lattice plane, facilitating atomic force microscope imaging of the lattice.

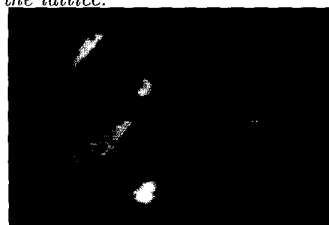


Figure 6: A non-computational DNA tiling formed by sets of two types of TAO tiles. parallelized.

2.4 Two Dimensional DNA Tiling Assemblies. Recently Winfree and Seeman have demonstrated the use of DX tiles to construct 2D periodic lattices consisting of up to a hundred thousand DX units [Winfree, et al 98] as observed by atomic force microscopy² The surface features are readily programmed [Winfree et al., 98; Liu et al., 99; Mao, et al 99]. (See Figure 5.) In addition, [LaBean et al, 99] constructed produced tiling arrays (see Figure 6) composed of DNA triple crossover molecules (TX); these appear to assemble at least as readily as DX tiles.

These tiling assemblies had no fixed limit on their size. [Reif97] introduced the concept of a *nano-frame*, which is a self-assembled nanostructure that constrains the subsequent timing assembly (e.g., to a fixed size rectangle). Alternatively, a tiling assembly might be designed to be *self-delimitating* (growing to only a fixed size) by the choice of tile pads that essentially 'count' to their intended boundaries in the dimensions to be delimited.

2.5 Three Dimensional DNA Tiling Assemblies.

There are a number of possible methods for constructing 3D periodic (non-computational) tilings. For example, stable tiling arrays with well-defined helices that come out of the plane (e.g., the TX tiling array constructed in [LaBean et al, 99]) may lead to ways to provide 3D tiling assemblies.

3 The Kinetics and Error Control in Self-Assembled Tiling Assemblies

3.1 Kinetics of Self-Assembled Tiling Assemblies.

In spite of an extensive literature on the kinetics of the assembly of regular crystalline lattices, the fundamental thermodynamic and kinetic aspects of self-assembly of tiling assemblies For example, it is not yet known the affect of distinct tile concentrations and different rela-

²An atomic force microscope [AFM] is a mechanical scanning device that provides images of molecular structures laying on a flat 2D plate.

tive numbers of tiles, and the possible application of Le Chatelier's principle.

Winfree [W98] developed computer simulation of tiling self-assemblies. This software makes a discrete time simulation of the tiling assembly processes, using approximate probabilities for the insertion or removal individual tiles from the assembly. These simulations provide an approximation to the kinetics of self-assembly chemistry. Using this software as a basis, Guangwei Yuan at Duke developed improved simulation software with a Java interface (<http://www.cs.duke.edu/~yuan/gw/project/test.HTML>) for a number of example tilings, such as string tilings for integer addition and XOR computations. This simulation software was recently speed up by use of an improved method for computing on/of likelihood, as suggested by Winfree.

The meso-scale tiling experiments described in Section 1 have used mechanical agitation with shakers to provide a temperature setting for the assembly kinetics (that is, a temperature setting is made by fixing the rate and intensity of shaker agitation). These meso-scale tilings also have potential to illustrate fundamental thermodynamic and kinetic aspects of self-assembly chemistry.

3.2 Error Control in Self-Assembled Tiling Assemblies. As stated above, two dimensional self-assembled *non-computational* tilings have been demonstrated (and imaged via atom force microscopy) that involve up to a hundred thousand tiles. Certain of these appear to suffer from relatively low defect rates, perhaps in the order of less than a fraction of a percentage or less. The factors influencing these defect rates are not yet well understood and there are no known estimates on the error-rates for self-assembled *computation* tilings, since such tilings have been achieved only very recently and have only been done on a very small scale (error rates appear to be less than 5% [Mao et al 00]). There is reason (see the construction of a potential assembly blockage described in [Reif, 98]) to believe that in computational tilings, defect errors may be more prevalent; and moreover, they can have catastrophic effects on the computation. Experiments need to be done to determine the error rates of the various types of self-assembly reactions, both computational and non-computational.

There are a number of possible methods to decrease errors in DNA tilings. It is as yet uncertain which methods will turn out to be effective and it is likely that a combination of at least a few of the following methods will prove most effective.

(a) Error Control by Annealing Temperature Variation. This is a well known technique used in hybridization and also crystallization experiments. It is likely that this will provide some decrease in defect rates at the expense in increased overall annealing time duration. In the context of DNA tiling lattices, the parameters for the temperature variation that minimize defects have

not yet been determined.

(b) Error Control by Improved Sequence Specificity of DNA Annealing. The most obvious methodology here is to improve the choice of the DNA words used for tile pads (that is, to decrease the likelihood of incorrect hybridizations from non-matching pads). DNA word design software for DNA tiles was developed by Winfree. This software has recently been improved by Horatiu Voicu at Duke University (see <http://www.cs.duke.edu/~hvoicu/app.html>) to include more realistic models of DNA hybridization, and was also speed up by use of a technique of Rajasakaran and Reif [RR95] known as nested annealing. Another possible approach is to use the observation and experimental evidence of [Herschlag 91] that stressed DNA molecules can have much higher hybridization fidelity (sequence specificity) than a relaxed molecule. This would entail redesigning DNA tiles, so their pads are strained single stranded loop segments with higher sequence specificity, or by the use of stressed DNA motifs known as "PX dumbbells" [Shen, Z. Ph.D. Thesis, NYU, 1999].

(c) Error Control by Redundancy. There are a number of ways to introduce redundancy into a computational tiling assembly. One simple method that can be developed for linear tiling assemblies, is to replace each tile with a stack of three tiles executing the same function, and then add additional tiles that essentially 'vote' on the pad associations associated with these redundant tiles. This results in a tiling of increased complexity but still linear size. This error resistant design can easily be applied to the integer addition linear tiling described above, and similar redundancy methods may be applied to higher dimension tilings.

(d) Error Control by Free Versus Step-wise Assembly. Self-assembly may be restricted so that certain assembly reactions can proceed only after others have been completed (*serial (or step-wise) self-assembly*). Alternatively, self-assembly reactions may be limited by no such restrictions (*free self-assembly*). It is expected, but unproven, that free self-assembly is faster than serial self-assembly. [Reif, 98] suggested the use of serial self-assembly to decrease errors in self-assembly. There is not yet any experimental data on the error rates of self-assembly reactions and error control/repair of 'self-assembly' versus 'serial-assembly'. To decrease the human effort in serial assembly, assembly steps might be executed automatically with the use of a robotic machines (E.g., the Nanogen machine, which employs a chip that contains DNA sequences above electrodes. Tile components hybridized to these DNA sequences can be released in sequence by making the electrode sufficiently negative.).

(e) Use of DNA Lattices as a Reactive Substrate for Error Repair. DX complexes and lattices have been used successfully as substrates for enzymatic reactions in-

cluding restriction cleavage and ligation of exposed hairpins attached to the tiles [Liu99a]. One approach is the use of DNA lattices to execute a broader class of reactions. For example, if restriction enzymes, topoisomerases or site-specific recombinases can be shown to operate on exposed portions of the DNA lattices, then it may be possible to modify the topology and geometry of the DNA lattice. This may aid in the DNA tiling computations described above, for example by providing mechanisms for error repair in DNA tiling computations. (Note: as mentioned above, this approach may also be of use for recycling of the component ssDNA for the next computation cycles.)

4 Applications of Non-Computational DNA Tiling Arrays

We now identify some further technological impacts of non-computational DNA assemblies; particularly their use as substrates for surface chemistry and molecular electronics, robotics. Many of these applications are dependant on the development of the appropriate attachment chemistry between DNA and the molecules attached to the arrays.

(4.1) Tiling Assemblies with Molecular Motors. Several types of molecules are known to couple chemical energy to the generation mechanical force, thereby functioning as molecular motors. Possible schemes for molecular motors include:

(a) Re-Engineering Biological Molecular Motors. Cells make use of a variety of such motor-like devices in processes such as mitosis. The best characterized of these fall into three categories.

(i) *ATP synthase and ADP* acts as a rotary motor, coupling proton flux through a membrane with the phosphorylation of ADP to ATP. The F1 component of ATP synthase can also be run in reverse, coupling hydrolysis of one ATP molecule to 120 B0 of rotation about the motor axis.

(ii) *Myosin* acts as a molecular running machine, skipping many steps along an actin filament with each molecule of ATP consumed. All of these motors are modular and can be re-engineered to accomplish linear or rotational motion of essentially any type of molecular component.

(iii) *Kinesin* acts as a molecular walking machine, translocating itself (and any attached components) in step-wise fashion along a microtubule. Each step along the microtubule consumes one ATP molecule.

Construction of these biological molecular motors and their linking chemistry to DNA arrays. These motors are composed of proteins with well known transcription sequences. There are also well known proteins (binding proteins) that provide linking chemistry to DNA. Hence it seems feasible that these molecular motors and attached linking elements may be synthesized from sequences obtained by concatenation of these transcription sequences. [Bachand, et al., 1999 and 2000], describes a biomolecular motor constructed of expressed ADP protein [Monte-

magno, et al, 1998 and 1999] with an attached [Soong, et al, 1999] silicon arm.

(b) DNA Motors. The Seeman laboratory made a DNA construction of a mechanical device capable of controlled movement [Mao, et al 99a]. This device consists of two DX molecules connected by a DNA double helix that contains a segment of DNA that can be converted to the left-handed Z-DNA structure. In B-promoting conditions, the two unconnected helices of the device are on the same side of the connecting helix, but they are on opposite sides in Z-promoting conditions. This results in an apparent rotary motion of about a half-revolution, leading to atomic displacements ranging from 2 to 6 nm, depending on the location of the atom relative to the axis of the stationary helix. This motion has been demonstrated by fluorescent resonance energy transfer (FRET). It is important to point out that the device based on the B-Z transition is only a prototype that was used to learn how to characterize motion in DNA systems. It lacks programmability, except to the limited extent that one can orient the two DX molecules at a variety of relative torsion angles in the B-state. Thus, all of the molecules must be in either the B-state or in the Z-state, assuming one has robust chemical control.

These molecular motors might be combined with the 2-D arrays, to achieve an array of devices (This has not been possible to do with the DX system, since it is most convenient there for the pivoting part of the system to point normal to the array. However, the TX system does not have this difficulty.). As an example, an array with attached kinesin may provide for the movement of objects across the surface of a two dimensional tiling array, similar to a conveyer belt, and this may be the basis of a transport system (*a molecular conveyer belt*) for molecular objects.

Programmable Sequence-Specific Control of DNA Mechanical Motion. However, such an array of molecular motors would be more useful if they can be selectively controlled. Such a system would lead to the ability to manipulate specific molecules and more generally, to do chemistry at chemically identical but spatially distinct sites. Because it couples a series of distinct structural states with programmability, such a system offers the potential of direct route to molecular robotics. The Seeman laboratory is developing a related system based on the paranemic crossover (PX) system, which leads to sequence-specific nanomechanical motion. It may be switched readily between two discrete states, PX or JX, in which the helices at one end of the molecule reverse positions in the transition between states. An array of these molecular devices would contain individually programmed PX/JX molecules, whose conformational state would be amenable to specific reversal (or not, depending on the program) from cycle to cycle. A DNA array with programmability of this sort may offer a mechanism

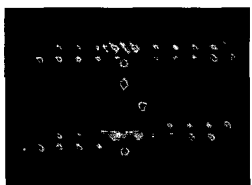


Figure 7: A prototype DNA nanomechanical device.



Figure 8: The Tour-Reed molecular electronic diode. to do DNA computation of arrays whose elements (the tiles) hold state, as discussed in the next section.

4.2 Application to Layout of Molecular-Scale Circuit Components. Molecular-scale circuits have the potential of replacing the traditional microelectronics with densities up to millions of times current circuit densities. There have been a number of recent efforts to design molecular circuit components ([Petty et al 95] [Aviram,Ratner98]). Tour at Rice Univ. in collaboration with Reed at Yale have designed and demonstrated [Chen et al 99] organic molecules (see Figure 7) that act as conducting wires [Reed et al.97],[Zhou99] and also rectifying diodes (showing negative differential resistance (NDR), and as well as [CRR+,99], [RCR+,00], and have the potential to provide dynamic random access memory (DRAM) cells. These generally use $\sim 1,000$ molecules per device, but they have also addressed single molecules and recorded current through single molecules [BAC+96], [RZM+97]. These molecular electronic components make conformational changes when they do electrical switching. One key open problem in molecular electronics is to develop molecular electronic components that exhibit restoration of a signal to binary values; one possible approach may be to make use of multi-component assemblies that exhibit cooperative thresholding.

The Molecular Circuit Assembly Problem: This key problem is to develop methods for assembling these molecular electronic components into a molecular scale circuit. Progress in the molecular circuit assembly problem could have revolutionary impact on the electronic industry, since it is one of the key problems delaying the development of molecular-scale circuits.

Top-down techniques versus bottom-up approaches. The usual approach of laying out circuits by top-down techniques (e.g., lithography) may not be practical at the molecular scale; instead bottom-up approaches (e.g., self-assembly) may need to be used. Hence this may be a key area of application of DNA tiling assemblies. There are a number of possible methods for the selective attachment of the molecular electronic components to particular tiles of the DNA tiling array, using annealing.

(i) *linking chemistry between DNA and molecular electronics.* Tour and Bunz recently prepared DNA-linked systems where the DNA could serve as a selective assem-

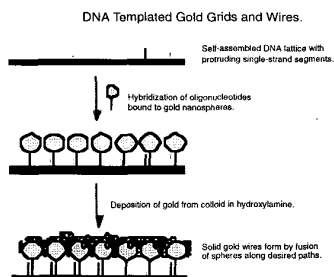


Figure 9: Diffusion of gold on beads to form molecular-scale gold wires.

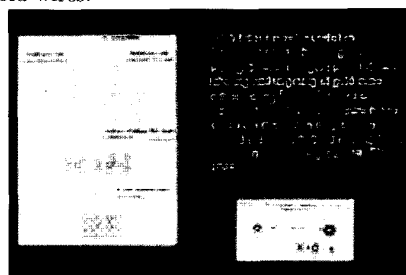


Figure 10: A scheme for molecular-scale gold wires. by glue for device configurations [WST+00].

(ii) *The use of gold beads.* In this approach, DNA strands attached to the gold beads can hybridize at selected locations of the arrays, and the molecular electronics components may self-assemble between the gold beads. Also, DNA lattices may be useful as a foundation upon which to grow nano-scale gold wires. This might be done by depositions of gold from colloid onto nanoparticles immobilized on DNA tiling lattices. (See Figures 8 and 9.) Molecular probe devices may be used to test the electrical properties of the resulting molecular circuit attached to the DNA tiling array. *Computational* lattices (as opposed to regular, non-computational lattices), may also be employed to provide for the layout of highly complex circuits, e.g., the layout of the electronic components of an arithmetic unit. (Other related approaches for positioning of molecular electronic molecules without lithography include that of [Bumm, et al., 1999, 2000], which describes the use of directed self-assembly of molecular terrace structures in organic monolayers.)

5 Conclusion

We have discussed the potential advantages of self-assembly techniques for DNA computation; particularly the decreased number of laboratory steps required. We also discussed the potential broader technological impacts of DNA tiling lattices and identify some further possible applications. The chief difficulties are that of error control and predictable kinetics, as described in the previous section. Nevertheless, the self-assembly of DNA tilings seems a very promising emerging method for molecular scale constructions and computation.

References: See <http://www.cs.duke.edu/~reif/paper/SELFASSEMBLE/references.ps>