Algorithm

Biology

Nonlinear Systems Biology and Design
Surface Design

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Material

Morphogenesis

Nonlinear

THE INTENT OF THIS PAPER IS TO JOINTLY INVESTIGATE FUNDAMENTAL PROCESSES IN LIVING SYSTEMS, THEIR POTENTIAL APPLICATION IN THE NOVEL DESIGN OF RESPONSIVE SURFACES AND SPATIAL STRUCTURES, AND THEIR APPLICABILITY IN BIOMEDICINE. Through the investigation of organotypic biological models designed to recapitulate breast tissue homeostasis and cancer, parallel models work to unfold the parametric logic of these biological and responsive membrane and scaffold structures, thereby revealing their deep interior logics. The result is an abstract surface architecture capable of responding dynamically to both environment (context) and to deeper interior programmed systems.

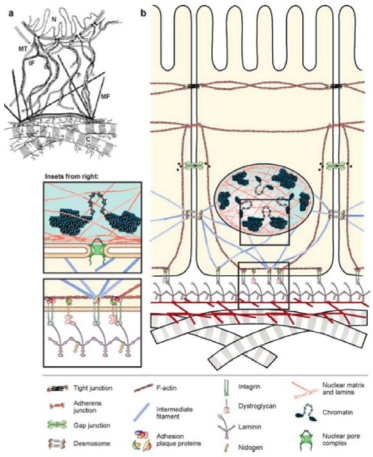


FIGURE 1. A MODEL OF DYNAMIC RECIPROCITY.

FIGURE 2. BUCKMINSTER FULLER WITH TENSEGRITY STRUCTURES.

1 Introduction

In "Nonlinear Systems Biology and Design: Surface Design", we argue that through analyses of tissues created within specialized 3-D designer microenvironments, the architect is afforded new ways of thinking about design through an understanding of dynamic feedback or reciprocity in context, albeit normal or pathological. Through parallel models, we aim to escape the trappings of biomimicry in favor of biosynthesis, where new models for surface architectures, membrane structures, and building systems are generated. One such project, researched by Wei Wang (PennDesign M.Arch. 2010 candidate), Misako Murata (PennDesign M.Arch. 2008, L.Arp 2009 candidate), Austin McInerny L.Arp. (University of Pennsylvania) Benjamin Vincent, Ph.D. (University of Dundee) and Agne Taraseviciute, Ph.D. (IME & University of Colorado), under the guidance of Jenny E. Sabin and Dr. Peter Lloyd Jones, seeks to quantify and spatialize breast tissue contour information through the design of its surface architecture in spherical and elliptical space. The project looks at the role of personal shape change as it relates to surface design. Here, the study of relationships found within the closed and open structure of tissues comprised of cell aggregates gives rise to an abstract understanding of form as it relates to dynamic boundary conditions and tissue mechanics. Through the use of digital and physical algorithms, geometric abstraction gives rise to the formation of dynamic spatial structures capable of shape shifting in context.

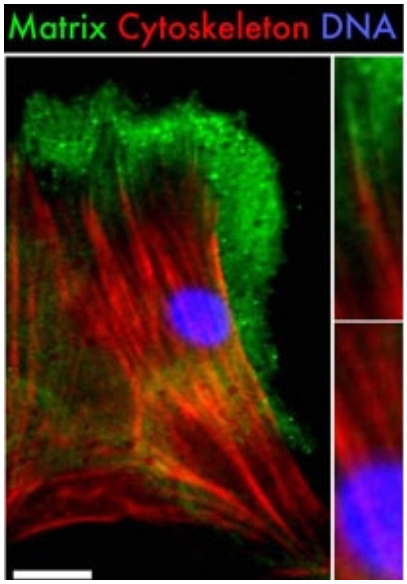
2 Surface Design Models

Pathologists and architects share similar concerns, such as how form is generated or lost, and this parallel is perhaps best reflected in the relationships that have emerged between our respective fields. Models borrowed from architects—such as tensegrity structures and geodesic (structures composed of spheres, triangles and hexagons) domes—have led to radical new insights into how living systems, including eukaryotic cells, tissues and whole organisms, are assembled and function, as well as to a new understanding of how the microecology of cells influences the genome. Similarly, models borrowed from biology, particularly regarding self- organization and the emergence of complex, non-linear global systems from simple local rules of organization, have led to the discovery of new forms and structural organizations in architectural design. Examples such as these demonstrate how attentive architectural and scientific practices can be to each other—particularly within architecture and biology, which are constantly reinventing and questioning themselves in a manner that is similar to the historic avant gardes, or in the face of new technologies.

Architects and structural engineers have historically looked to nature to design and build better shell and spatial structures. Cable nets have been inspired by the high strength-to-weight ratio of the spider web; pneumatic structures after soap bubbles; vaults after shells and eggs composed of hard and curved materials; and geodesics after radiolarian. The structural designer, Robert Le Ricolais, studied the tension networks inherent to radiolarian in order to understand the dynamic properties and qualities of closed and open "skeletal" structures. Le Ricolais professed that he had 'found no better discipline in this unpredictable problem of form than to observe the prodigies created by nature' (Le Ricolais 1973). Particularly interesting is his observation that in nature, the art of structure and form is where to place holes, 'all different in dimension and in distribution' (Le Ricolais 1973). This discovery lead to Le Ricolais' impossible desire to build with holes, to generate structures of 'zero weight and infinite span.' This seemingly contradictory statement shows us that in nature, we frequently find form that globally is extremely strong, yet is locally fragile. Le Ricolais argues for a higher level of (bio)synthesis. Why would we convert radiolarian structures into buildings? He exclaims, "Why should the Radiolarian help us to make money?" (Le Ricolais 1973). Robert Le Ricolais worked to unfold and eventually discover more intelligent translations and deeper relationships between architecture and science. Similarly, contemporary biology teaches the architect that context and dynamics count, leading to new models for building systems, structure, form and matter.

2.1 ARCHITECTURAL BIOLOGY: CONTEXT AND DYNAMICS

The fashionable ideology of ultra-Darwinism, which reduces organisms to little more than



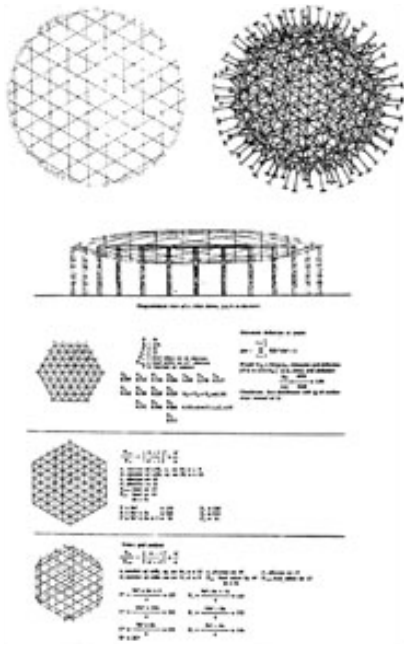


FIGURE 3. CELLS CAN BE VIEWED AS "HARD-WIRED" NETWORKS OF MOLECULAR STRUTS, WHICH EXTEND FROM THE EXTRACELLULAR SPACE TO THE DNA VIA THE CYTOSKELETON. AT THE PHYSICAL LEVEL, THIS MODEL IS REMARKABLY SIMILAR TO LE RICOLAIS' TRIHEX NETWORK STRUCTURES (BOTTOM).

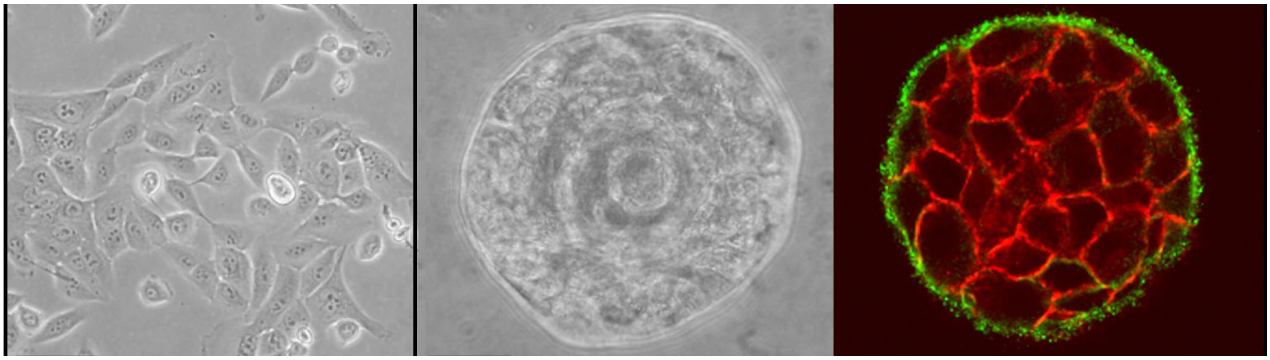
machines for the replication of DNA, is gradually being replaced by a more holistic trajectory in which life is considered to depend upon complex interactions that occur within cells, organisms, and with their micro- and macro-environment through time and space. By placing the cell, tissue or organism, rather than the gene at the center of life, a different perspective on the construction and dynamics of organismal architecture is beginning to emerge.

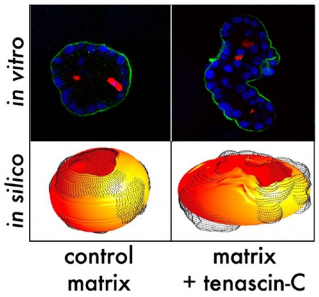
The idea that cells within tissues function as integrated architectural units that include their surrounding microenvironment was elegantly described by the developmental and cell biologist Paul Weiss in 1945...."the living units enmeshed in [the microenvironment—which includes the extracellular matrix (ECM)] .....bind them to the substratum. It thus confers upon what otherwise would be isolated units, the character of a coherent tissue" (Weiss 1945). Scientific descendents who advocate this type of model include Mina Bissell, who has refined this idea to suggest that a state of "Dynamic Reciprocity" exists between cells and their immediate microenvironment: "A dynamic reciprocity exists between the extracellular matrix on the one hand and the cytoskeleton [which supports translation of messenger RNA into protein] and the nuclear matrix [which associates with chromatin, the site of transcription of genes into messenger RNA] on the other hand. The extracellular matrix is postulated to exert physical and chemical influences on the geometry and the biochemistry of the cells via transmembrane receptors so as to alter the pattern of gene expression by changing the association of cytoskeleton with the mRNA and the interaction of chromatin with the nuclear matrix. This, in turn would affect the extracellular matrix, which would affect the cell..."], (Bissell 1982) and so on (Figure 1).

What is the evidence that cell and tissue architecture, specified by the microenvironment, forms part of a dynamic chemico-physical loop that signals to cells and their cargo genomes and back again? Mostly inspired by the works of Buckminster Fuller and Kenneth Snelson, tensegrity has been successfully transposed from architecture and sculpture to cell biology (Figure 2). Significantly, as early as 1935 in his article entitled "Le Toles Composees et leurs applications aux constructions metaliques legeres", Le Ricolais imagined a rapport of relationships in opposition, leading to the conclusion that there is a correlation between a mechanical principle and a geometric pattern (Nelson et al, 2006.). As with models of architectural tensegrity, tension in cellular tensegrity is continuously transmitted across all structures within the cell so that tension in one of the members, results in increased tension in members throughout the structure. How does this relationship relate to environmental influences on gene expression and cell behavior? Inside cells, a network of filaments extend throughout the cell exerting tension. In turn, this structure is linked to the extracellular matrix and to the nucleus via filaments that comprise the nuclear matrix. Thus, the cell can be viewed as a "hard-wired" parametric network of molecular struts, which extend from the extracellular space to the DNA via the cytoskeleton (Figure 3). If the cell and nucleus are physically connected by tensile filaments and not solely by a fluid cytoplasm, then chemical or physical stimulation of receptors [which interact with the matrix] at the cell surface should produce immediate structural changes deep inside the cell. Indeed, both actual and simulation models of tensegrity reveal how mechanical forces applied to the cell surface lead to realignment of cytoskeletal fibers/filaments and structures within the nucleus (where the genome is located). What is more, soluble biochemical reactions are known to take place on the solid-state cytoskeletal fiber bundles, indicating that changing extracellular matrix-dependent cytoskeletal geometry can modulate signaling to and from the genome. At the physical level, this model is remarkably similar to Le Ricolais' Trihex network structures, and to his Funicular Polygon of Revolution system, which is described by "connectivity of the compression system, and the chain action of the tension cables, acting as bundles of fibers" (Figure 3).

3 New Models

Novel insights arising from collaborations between architects and biologists will give rise to formerly unseen models for research, education and development in architectural and industrial design, biomedicine, nanotechnology, structural engineering and software devel-





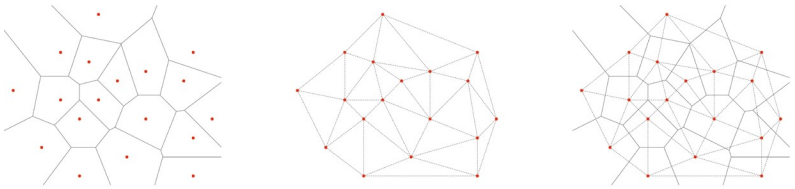


FIGURE 4. THIS DEPENDENCE ON THE EXTRACELLULAR MATRIX ENVIRONMENT FOR NORMAL BREAST STRUCTURE AND FUNCTION EXPLAINS WHY ISOLATED MAMMARY EPITHELIAL CELLS CULTIVATED ON HARD, 2-D, CHEMICALLY-INERT, SURFACES FAIL TO ACHIEVE A NORMAL FORM, EVEN THOUGH THEY POSSESS THE APPROPRIATE GENES THAT SHOULD ENABLE THEM TO DO THIS (FIGURE 4 LEFT PANEL). WHEN CULTIVATED WITHIN A COMPLIANT, 3-D EXTRACELLULAR MATRIX "FABRIC" WITHIN A TISSUE CULTURE DISH, HOWEVER, DUCTAL CELLS CAN BE INDUCED TO UNDERGO A NORMAL MORPHOGENETIC PROCESS (FIGURE 4 MIDDLE AND RIGHT PANELS).

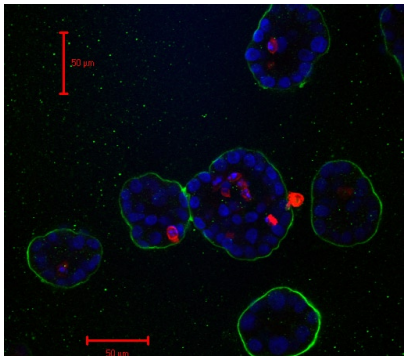
FIGURE 5. IMPORTANTLY, OUR STUDIES MAKE USE OF A COMPLEX 3-D MODEL OF BREAST MORPHOGENESIS AND CANCER IN WHICH CELLS ARE CULTURED IN A 3-D GEL MATRIX, EITHER WITH OR WITHOUT THE PRESENCE OF TENASCIN-C PROTEIN.

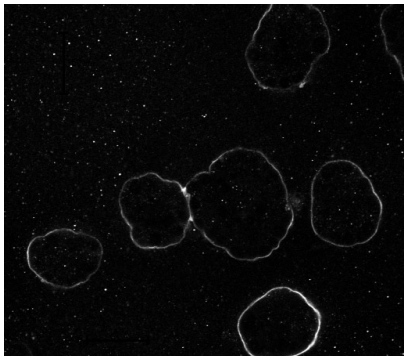
FIGURE 6. ALGORITHMIC TOOLS ASSIST WITH THE FILTERING AND EXTRACTION OF GEOMETRIC AND SITE-BASED INFORMATION.

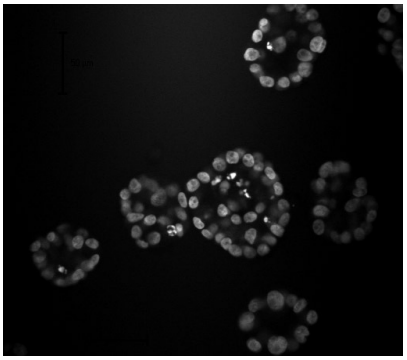
opment. These new models will be made intelligent through the study of code in context. Here, sets of relationships are defined by a blueprint of instructions or algorithms that are then altered and informed through program and especially environment, at all scales. Novel examples that come to mind are the transformable and deployable structures developed by Chuck Hoberman. These retractable roofs, chairs, tents, wall elements and even toys and medical tools are capable of transforming at multiple scales, adapting to diverse environments with varied functions through the use of a highly adaptable 3-D scissor mechanism. Hoberman Associates' work is centered on the fundamental idea that a designed object can transform the way a natural organism does. Hoberman argues that while the smooth transformation of size and shape is ubiquitous in the natural world, it is rare among man-made objects. Or, perhaps we might learn from the theoretical and visionary work of Karl Chu who exclaims that the future of architecture and design is in genetic engineering, biotechnology and universal computing. He argues that for the very first time, we are able to "think of a new kind of xenoarchitecture: an information labyrinth or, better still, a universal matrix that is self-generating and self-organizing with its own autonomy and will to being." We very well may be growing buildings through the design and mutation of code in the near future! Alternatively, perhaps we may turn to Cecil Balmond and the Advanced Geometry Unit at ARUP who explore the use of mathematical, physical-geometric and natural algorithms in architectural and structural design. Their spiral addition to the Victoria and Albert Museum's contemporary wing in collaboration with architect Daniel Libeskind, features an interlocking natural spiral structure and an external tiled façade generated from a mathematical model called the Fibonacci Sequence that forms fractal and branching figures. This mathematical mosaic moves from ornament to structure and back again. Examples such as these show how part-to-whole relationships drive assembly where the resultant geometric figure emerges through contextual understanding. Mutations in the generative code and the environment both intersect and interact to alter the blueprint or algorithm (literal and genomic) and new understandings emerge. What is it like to inhabit such a model? It demands a willingness to surrender to a process, to let loose a simple set of instructions, and to see how they are made intelligent and functional through mutations of transformation, feedback and context. It is a slight of hand moment where an intelligent architecture is clarified and we are allowed to enter.

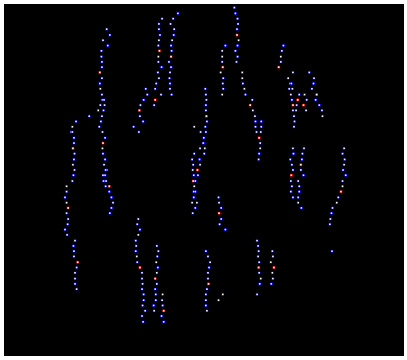
3.1 IME-PENNDESIGN LABSTUDIO: ONGOING RESEARCH BETWEEN PENNDESIGN, PATHOLOGY AND LABORATORY MEDICINE & THE IME

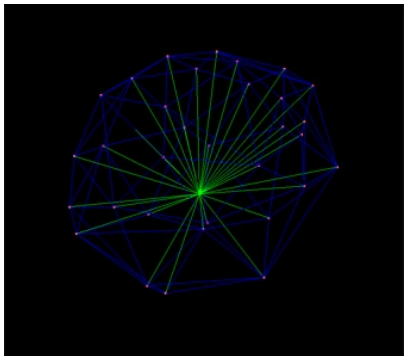
The aforementioned dialogues and processes have already been initiated via a LabStudio initiated in Spring 2007 by Peter Lloyd Jones and Jenny E. Sabin, conducted at the Institute for Medicine and Engineering, UPenn and the Nonlinear Systems Organization at PennDe-

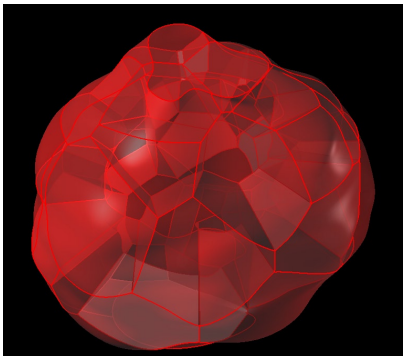


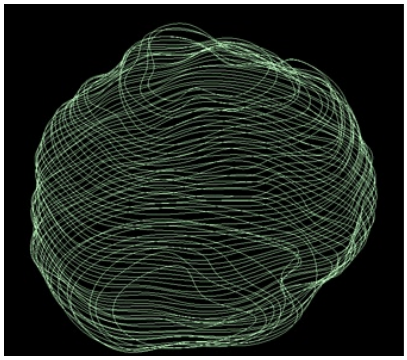


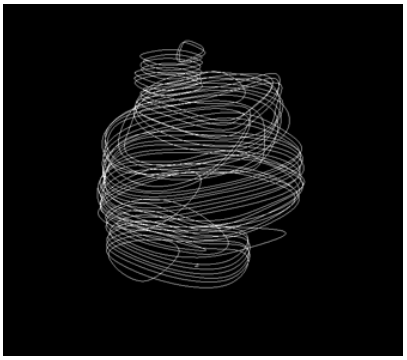


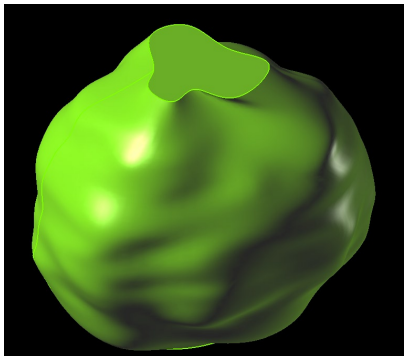


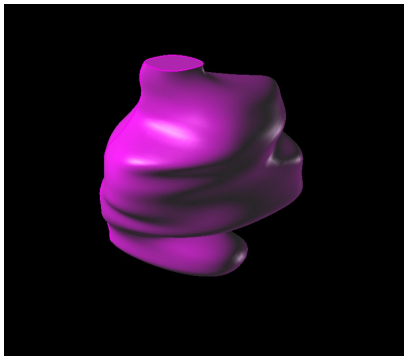


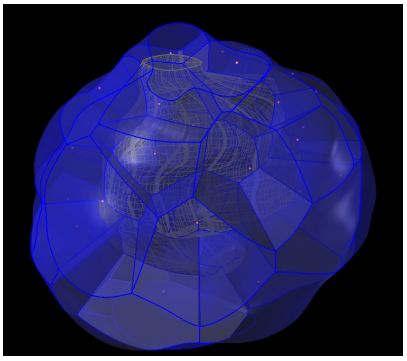












FIGURES 7,8,9. THE FIRST SERIES OF 63 IMAGES SHOW HOW CELLS ARE STACKED AND DISTRIBUTED BASED ON RELATIONSHIPS BETWEEN AN EXTERNAL MEMBRANE CALLED A BASEMENT MEMBRANE (SHOWN IN GREEN) AND THE FORMATION OF AN INTERNAL LUMINAL VOID. COLOR CHANNELS ARE USED TO SELECT PIXEL-BASED INFORMATION FROM THE ORIGINAL IMAGE SECTIONS.

FIGURES 10-12. THE INDIVIDUAL SECTIONS OF TRACED POINTS ARE SYNTHESIZED BY LINEAR STACKING WITH A DEVIATION OF 1 MICROMETER. THE BLUE MESH IS BASED ON THE DELAUNAY ALGORITHM. THIS MESH STRUCTURE MODELS THE LINEAR CONNECTIVITY WITHIN ACINI. THE RED MESH MODELS GEOMETRIC INFORMATION FILTERED BY THE VORONOI ALGORITHM.

FIGURES 13,14. THE NEXT STEP IS TO RECONSTRUCT THE SURFACE OF THE EXTERIOR BASEMENT MEMBRANE (LEFT) AND THE INNER LUMINAL VOID (RIGHT).

FIGURES 15,16. A SINGLE LAYER OF SMOOTH NURBS-BASED SURFACE IS GENERATED FROM THE CONTOURS TRACED FROM THE ORIGINAL IMAGES.

FIGURE 17. THE THIRD STEP IS TO UTILIZE THE CENTROID AS A RESOURCE, THE BASEMENT MEMBRANE AND INNER SURFACE AS BOUNDARIES OR LIMITS AND TO BUILD A CRYSTAL-SHAPED CELLULAR STRUCTURE TO ABSTRACT FORMATION OF ACINI. THE LOGIC OF LOCATING AND FORMING THE BOUNDARY FOR NEIGHBORING CELLS IS AGAIN BASED ON THE 3-D VORONOI DIAGRAM, WITHIN WHICH A FLAT SURFACE IS GENERATED IN AN EQUAL DISTANT POSITION FROM NEIGHBORING POINTS. FIGURES 18-23. CASE 2 WITH TN-C.

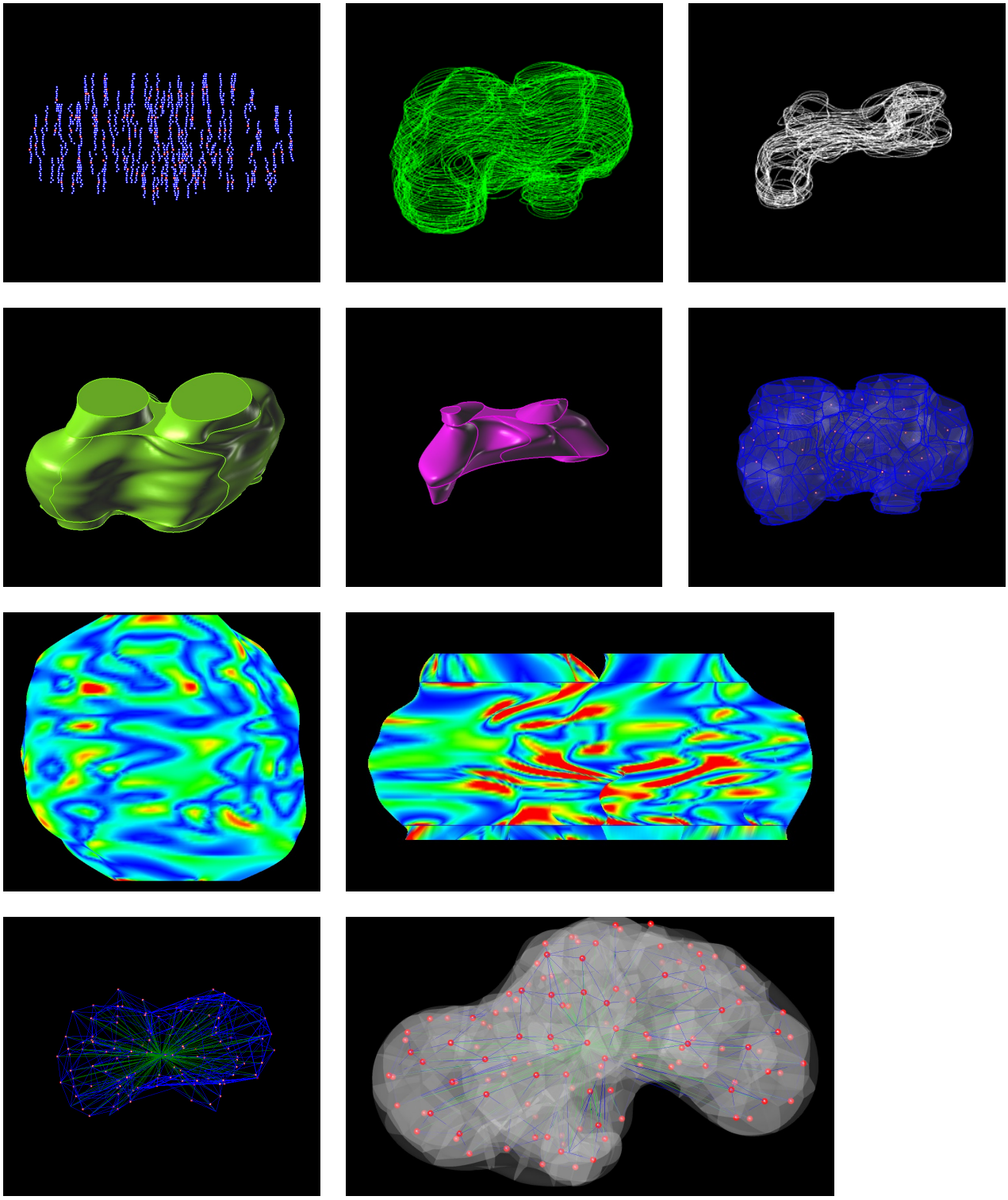


FIGURE 18. STACKED NUCLEI POINTS (UPPER LEFT)

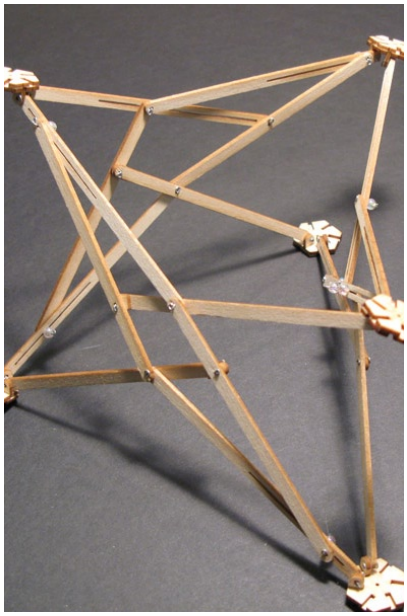
FIGURE 19. STACKED CONTOURS GENERATED FROM EXTERIOR POINTS (UPPER MIDDLE); FIGURE 20. STACKED CONTOURS GENERATED FROM INTERIOR POINTS (UPPER RIGHT)

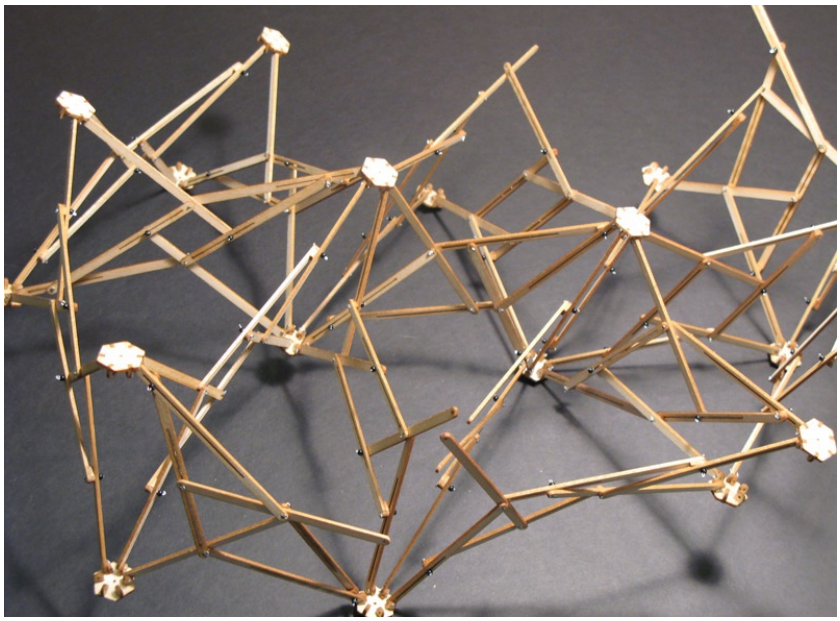
FIGURE 21. EXTERIOR SMOOTH SURFACE (LOWER LEFT)

FIGURE 22. INTERIOR SMOOTH SURFACE (LOWER MIDDLE); FIGURE 23. VORONOI MESH STRUCTURE, NUCLEI AND INTERIOR STRUCTURE (LOWER RIGHT).

FIGURES 24, 25. THE FIRST COMPARISON IS FOCUSED ON SURFACE ROUGHNESS, WHICH WE KNOW INCREASES IN BREAST CELLS TREATED WITH TN-C. SURFACE ROUGHNESS IS CALCULATED BY THE SLOPE OF THE TANGENT PLANE ON SPECIFIC POINTS ON THE SURFACE. THE RANGE OF ROUGHNESS IS VISUALIZED THROUGH A COLOR SPECTRUM. RED INDICATES ROUGHNESS AND BLUE INDICATES FLATNESS. CONTROL (MIDDLE DIAGRAM) AND TN-C TREATED (RIGHT).

FIGURES 26, 27. THE THIRD COMPARISON IS FOCUSED ON SURFACE TENSION.





sign. The LabStudio is comprised of architecture graduate students from PennDesign and graduate students and post-doctoral fellows at the Institute for Medicine and Engineering. To begin to explore models in complex physical material systems and surface and spatial structures, we have used the human mammary gland as a model system.

3.2 THE MAMMARY GLAND AS A MODEL OF ARCHITECTURAL CONNECTIVITY

The physiologic function of the normal adult mammary gland is to produce milk upon demand, and to cease this process following weaning. Accordingly, the mammary gland must expand, differentiate and then regress in response to its global and local environment. Indeed, at puberty, a rudimentary duct or tube made from epithelial cells transforms into a fractal, tree-like structure, and with pregnancy, the structure of the mammary gland dramatically changes once more. In this instance, a specialized surface membrane structure, made of extracellular matrix proteins is produced, and this matrix interacts with adjacent cells to promote a massive expansion of the ductal tree. Following birth, milk must be secreted from the ductal cells into a central hollow luminal space; creation of this space occurs via a cellular suicide program within a sub-population of ductal cells that no longer remain in contact with the extracellular matrix. Thus, by controlling cell growth, differentiation and survival, the extracellular matrix gives rise to boundaries and space, resulting in extraordinary overall form (Figure 4). This dependence on the extracellular matrix environment for normal breast structure and function explains why isolated mammary epithelial cells cultivated on hard, 2-D, chemically-inert, surfaces fail to differentiate, even though they possess the appropriate genes that allow them to do this (Figure 4). When cultivated within a 3-D extracellular matrix, however, ductal cells undergo a normal morphogenetic process. In contrast, with cancer, the integrity and quality of the extracellular matrix changes, resulting in inappropriate growth responses to this modified matrix environment. Collectively, these and other events lead to the loss of normal tissue architecture, a cardinal feature, and in fact a driving force in breast cancer. Clearly, modeling the behavior of tissues in 3-D represents an important step in understanding their behavior in development and disease.

One of the crucial lessons arising from the above example is that in order for the model to reproduce relevant characteristics of the system being studied, the model has to share similar complexities and constraints of the original system. The design of these constraints, based on logic, intuition and experience, becomes the nuanced role of the scientist. To approach this, we are studying the interaction of human mammary epithelial cells with the extracellular matrix components, laminin and tenascin-C. Normal cells rest on a layer of laminin, whereas the cells surrounding breast cells produce tenascin-C. Impor-

FIGURES 28, 29. DEPLOYABLE STRUCTURES. STUDY MODELS BY MISAKO MURATA.

tantly, we have shown that tenascin-C not only alters 3-D tissue architecture, but that it actively promotes tumor formation, via its ability to induce the expression of cancer-associated genes. To determine the magnitude of these changes, an imaging algorithm was developed for generating 3-D renditions of mammary acini, which were then used to assess and quantify acinar topography and volume (Figure 5). The abstraction of mammary acini structures is difficult using conventional cell biological computational tools. To resolve this, we have initiated a project to investigate new concepts and techniques that allow further examination of part-to-whole relationships in the normal mammary epithelium, and in one that is exposed to tenascin-C . It is hoped that these investigations will lead to novel scientific hypotheses and architectural designs.

3.3 NEW CONCEPTS & TECHNIQUES: SURFACE DESIGN

The project that we describe seeks to quantify and spatialize mammary epithelial tissue contour information through the design of its surface architecture in spherical and elliptical space. The project entails the reconstruction of the mammary epithelium from 2-D Z-stack images into abstractions that describe the interior logic of tissue formation and development.

In this surface design project, we are working with physical and digital algorithms in two different trajectories. The first makes use of digital algorithms: Delaunay Tessellation and the Voronoi diagram. A second trajectory incorporates deployable structures as a testing ground for programmatic information gleaned from the biological model of the study: the human mammary gland. We will begin with the first trajectory.

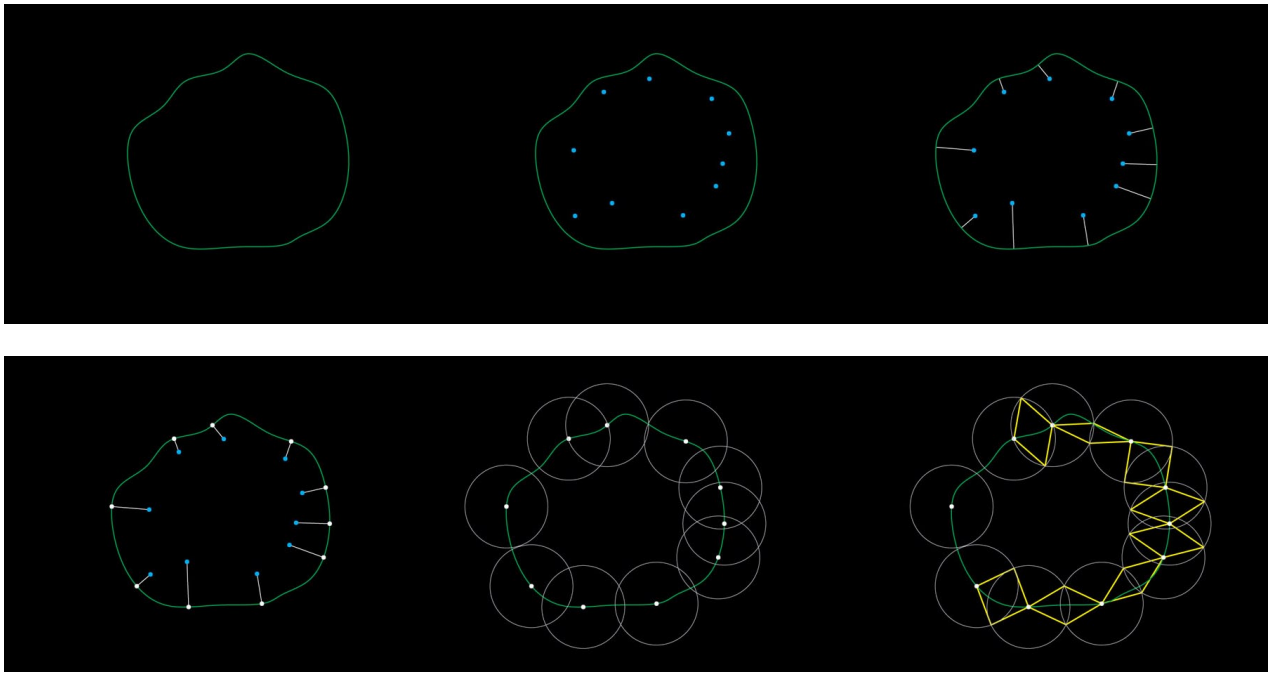
The Delaunay Tessellation is a dual tessellation of the Voronoi diagram. A Voronoi diagram is a geometric structure that represents proximity information about a set of points or objects. Given a set of sites or objects, the plane is partitioned by assigning to each point its nearest site. The points, whose nearest site is not unique, form the Voronoi diagram. That is, the points on the Voronoi diagram are equidistant to two or more sites. The Delaunay triangulation of a point set is a collection of edges satisfying an "empty circle" property: for each edge we can find a circle containing the edge's endpoints but not containing any other points. The Delaunay triangulation is the dual structure of the Voronoi diagram in R^2. By dual, we mean to draw a line segment between two Voronoi vertices if their Voronoi polygons have a common edge, or in more mathematical terminology: there is a natural bisection between the two, which reverses the face inclusions. The circumcircle of a Delaunay triangle is called a Delaunay circle (Figure 6). This is not all that dissimilar to Le Ricolais' investigations into bimorphism, or the combination of a form with its dual. The planar image of a 3-D structure can be found by graphically representing the forces in its members, once the reactions at boundaries have been determined. This planar image is a structure's dual.

4 Methods

Early modeling investigations for both trajectories in this project include the analysis of several image Z-stacks derived via confocal microscopy. The first series of 63 images show how cells are stacked and distributed based on relationships between an external surface of the acini, called a basement membrane, the nuclei, which houses the genome, and the formation of an internal luminal void (Figure 7).

The first series of 63 images show how cells are stacked and distributed based on relationships between an external membrane called a basement membrane (shown in green) and the formation of an internal luminal void. Color channels are used to select pixel-based information from the original image sections.

The blue dots represent the location of the nuclei, while the red lines indicate the boundaries between neighboring cells. The geometrical centroids of each nucleus are used as reference points to regenerate the structure into a 3D parametric mesh model. The basement membrane (green areas) and the boundary of the inner void are traced in a 3D modeling program. Color channels are used to select pixel-based information from the original image sections (Figures 8,9). The processing of pixel-based data enables a more



accurate description of the location of the centroid of each nuclei and a clearer definition of the boundary condition.

All 63 sections are mapped and reconstructed, using both the Delaunay and Voronoi meshes. The individual sections of traced points and curves are synthesized by linear stacking with a deviation of 1 micrometer (Figure 10). The blue mesh is based on the Delaunay algorithm (Figure 11). This structure models the linear connectivity within acini. Connections are made between acini through shortest path or nearest neighbor information. The red mesh model depicts geometric information filtered by the Voronoi algorithm (Figure 12). This filter visualizes moments of equilibrium found at boundaries under variable pressures. A third algorithm is used which is based on the same geometric filter called the Voronoi Diagram, but this final step uses a 3D Voronoi Diagram. This allows for the modeling of the space and structure of equal balanced boundaries between point sets. The algorithm follows the same logic as the 2D Voronoi, but nearest neighbor paths shift from straight-line connections to equal distant planes. The red enclosure models the boundaries of cells within the tissue.

Within the aforementioned system, we are interested in how the Delaunay and Voronoi filters may aid in the modeling and description of the acini's formation, in terms of minimized energy and dynamics. Here, parametric relationships describe the distribution of forces throughout the structure. For example, a tension deferential exerted upon the external surface tells us about the logic and formation of interior structures. This in turn, provides new insight into the novel design of abstract shell and spatial structures composed of complex surfaces with dynamic interior structures. Subtle adjustments made to interior structures adjust membrane behavior and performance and vice versa.

4.1 METHODS: PART 2

In more advanced modeling stages, the exterior basement membrane and the inner luminal void are reconstructed in 3D digital space from the data abstracted from the confocal image stacks (Figures 13,14). A single layer of smooth nurbs-based surface is generated from the contours traced from the original images (Figures 15,16).

The third step is to utilize the centroid of the acinus as a resource, the basement membrane and inner surface as boundaries or limits, and to build a crystal-shaped cellular and spatial structure to abstract and better understand the formation of acini. The logic of locating and forming the boundary for neighboring cells is again based on the 3D Voronoi diagram, within which a flat surface is generated in an equal distant position from neigh-

FIGURES 30, 31. PROGRAMMING OF THE 2D AND 3D MECHANISMS WITH INFORMATION FROM THE MODEL OF STUDY: THE HUMAN MAMMARY GLAND.

boring points. The crystal structure encloses certain points and is the result of a series of calculations based on distance and point-to-point orientation. A single local crystal module is the result of the synthesis of global behavior across the entire structure (Figure 17). The logic that drives the behavior of the surface boundaries activate, limit and control the formation of both individual units and the entire shell structure.

In order to gain more information about the formation of the "crystalline" and spatial structural forms, their surface structures and their parametric relationships, two experimental conditions were modeled and compared—case 1 is a normal control, as described above, whereas case 2 represents acini exposed to both laminin and tenascin-C (i.e,. the tumor-like or diseased microenvironment) as described below (Figures 18-23).

The first comparison focused on surface roughness, which increases in breast epithelial cultures treated with TN-C. Surface roughness is calculated by the slope of the tangent plane on specific points on the surface. The range of roughness is visualized through a color spectrum. Red indicates roughness and blue indicates a smoother surface. In the case of the control models, the surfaces are relatively smooth whereas the inclusion of TN-C increases the amount and degree of surface roughness (Figures 24,25).

The second comparison examines distance, packing behavior and connectivity between neighboring nuclei. A 3D Delaunay system that is projected to the outer basement membrane surface is used to frame the local connectivity, and the distances between neighboring nuclei can be measured.

The third comparison focuses upon surface tension. Based upon observation, the tension in the controlled case is relatively evenly distributed, while in the diseased scenario, the tension shifts dramatically. Collectively, these findings may be relevant to breast tumorigenesis in which loss of basement membrane continuity, cell packing, and changes in tensional homeostasis in response to alterations in the extracellular matrix and gene expression are known to play a central role (Figures 26,27). Further, all three comparison studies allow us to envisage potential parallel models where such environmentally impacted crystalline structures may take on new constraints within an architectural context and at different length scales.

5 Adherens junctions as a mechanism to reveal novel forms of structural deployability

In the second trajectory of the surface design project, deployable structures are incorporated as a testing ground to better study junctions between cell surfaces. Deployable structures are composed of three key elements: structure, mechanisms and the programming of such mechanisms. In our case, the information programmed and transmitted through the specified mechanisms comes directly from the biological model being studied.

Adherens junctions are specialized forms of adhesive contacts important for tissue organization in developing and adult organisms, including construction and maintenance of the normal, adult mammary epithelium. Cadherins, a major component of adherens junctions, form protein complexes with cytoplasmic proteins that convert the binding capacity of the extracellular domain into stable cell adhesion between adjacent cells and their surrounding extracellular matrix. The extracellular and intracellular domains of cadherins providing cytoskeletal anchorage between cells, coupling cytoskeletal force generation to strongly adhere sites on the cell surface and the regulation of intracellular signaling events. With breast cancer, however, the stability of these junctions is compromised. In fact, loss of cadherin-based junctions may lead to cancer progression. Since tenascin-C affects cell-cell junctions at the level of actin cytoskeleton, we aimed to understand how this structural and functional cellular component changes between adjacent cells in control and tenascin-C treated 3-D organotypic normal, mammary epithelial cell cultures with the hope that these studies might reveal novel modes of structural deployability that would be scalable from the micron to meter levels.

5.1 METHODS 2

Filopodia are thin projections from a cell's cyctoplasmic edge containing actin filaments. Central to cell-to-cell adhesion, recent research has found that at coincident membrane

sites, filopodia reach and penetrate into adjacent cells linking them together. Over time, this causes the actin cytoskeleton to remodel. Adherens proteins are expressed on epithelial cells near the apex of the surface showing basal lateral polarity. In our investigation, one hypothesis deals with the degradation of the basal lateral polarity in TN-C treated cells. Current knowledge lacks the understanding of the actin dynamics associated with intercellular adhesion. Therefore, certain interactions are hypothesized based on available data for analysis. The research was used to define possible variables that could be manipulated, abstracted and tested in newly designed deployable structures.

To further reveal the relationships between cell-basement membrane connections and cell packing qualities, points of intersection where the cells touch the basement membrane, were extracted and abstracted to visualize the geographical relationships between these points of contact. When applying the deployable structure model, the varying range, quality and duration of each deployable performance varies within the normal and diseased contexts. Further, by programming common 2D and 3D scissor mechanisms with this biological information, we are able to generate differentiated deployable structures. Here, the geometry of the deployable structure transforms from a strictly abstract and predictable state to one that acquires variability and novel response mechanisms to environmental constraints. Below are two images of the described deployable structures (Figures 28,29).

To change the packing density in a typical 2D deployable structure, we can change either the distribution of points within the model being studied or the length of the lines connecting neighboring points. Both parameters contribute to the formation and duration of a deployable connection, but they also reference different cell packing performances. In order to calculate the effective range of both parameters and the length of the basement membrane contour, we built these connection models for every Acini section. The diagrams below describe this process (Figures 30,31). Here, subtle adjustments to the exterior basement membrane change the degree and extent of each local deployment thus affecting the overall global behavior of the deployable structure.

6 Conclusion

How might the aforementioned modeling investigations enable new understandings in how a surface structure may respond dynamically to its environment and in turn be tuned by its deep interior structure through feedback mechanisms? By immersing oneself in biological design problems, such as those described above, and abstracting these biological relationships into code-driven parametric and associative models and tools, it is possible to gain new insights into how nature deals with dynamics, environment and feedback within cell and tissue structures. Certainly, we do not aim to generate a form or design a building after a cellular structure, but perhaps architects might learn from these biological models such that architecture acquires ‘tissueness’ or ‘cellness’ and is not merely ‘cell- or tissue-like’. We believe the tools produced and designed throughout this process will find potent alternative applications in architectural contexts. The abstract models described in this paper offer up novel approaches and methods for the design and fabrication of shell, spatial and deployable structures capable of shape shifting in alternative and scalable contexts.

Based upon our investigations, we posit that any future investigation between architecture and biology should require a consideration of models that capture and cultivate the dynamic reciprocity of the less obvious organic systems of architecture and the more obvious living complexities of biological systems. To address this, we ask whether architecture can take a cue from biology in matching the complexity of its generative design models to the very dynamic features of the living environment and organic milieu in which the architecture is a part, or, perhaps even attempt to build models which do more than merely problem solve structural difficulties, and explore the intricacies and organizational capacities of the diverse physical material systems from which it is constructed. Only then will we begin to move towards a more dynamic and volumetric model where surface architecture acquires connectivity, performance and time as embedded features. The result, as depicted in the examples explained in this paper, is the design of novel tools and the formation of

visionary surfaces and spatial structures capable of responding dynamically to both environment (context) and to deeper interior systems.

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