EPISTEMOLOGY OF CANCER GENOMIC SYSTEMS

A Discussion of the issues and principles related to the development of models for cellular dynamics of cancer cells.

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Contents

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1. ELEMENTS AND STRUCTURES

We will develop models of cellular systems with their genetic flows and from those models attempt to predict future behavior as well as ascertaining means and methods to alter unacceptable future behavior to a more benign state. Yet in so doing we will be attempting to abstract from nature what is necessary and ultimately ignoring what we believe is not. We will undoubtedly leave a great deal of what is essential behind, to only discover it again at a later point. Before taking the step in that direction we will lay out some boundaries of our human though process.

The purpose of this document is to lay out some basic principles that we believe should be included in model making. Models can often become paradigms, namely gold standard example of how things should be viewed. This paradigmatic approach may oftentimes be quite helpful in analysis and synthesis, yet if it is too simplistic or it fails to reflect the true underlying behavior then we can get badly lost in unfounded results.

On the other hand there is the problem of the wealth of data. Data is important but too much data can not only be overwhelming but it can be counterproductive if not destructive. For example, the microarray approach, we can find genes which now correlate with almost any cancer. That has some advantage but all too often it has a major disadvantage. For, we may not know whether it is cause or effect, whether it is just a random occurrence or something of significance, we may be just ignorant.

We will argue here that it is essential to have models of processes, to have an embodiment in some abstraction, which we can then validate our measurements. Furthermore the model should be predictive, namely we can use the model and from it reliably predict some outcome. Even more so, the model should have the capability to allow us to control the outcome as well, namely manage or eliminate aberrant behavior. As Dougherty (Epist Genom) notes:

The change brought about by the "new science" of the Sixteenth and Seventeenth Centuries is based on the integration of two principles: (1) design of experiments under constrained circumstances to extract specifically desired information; and (2) mathematical formulation of knowledge. The two principles arise from the two sides of the scientific problem, the source of knowledge and the representation of knowledge in the knower. Perhaps the greater revolution in knowledge is the design of experiments. One need only think of Archimedes' mathematical analyses of fluidics and mechanics to see that the ancients recognized the central role of mathematics, even if they did not understand that role in the modern sense. But the modern concept of experiment is a different matter altogether. The Greeks understood the role of observation, but not the idea of a controlled scientific experiment. Nor was this idea familiar to Ptolemy. It was Galileo who realized that Nature should not be observed au natural, but instead should be artificially constrained to focus on the phenomena of interest without the effects of confounding variables.

What Dougherty so masterfully observes is that to many degrees what we seen in genomics today are the approach comparable to Greek data gathering, collecting massive amounts of data without a validateable model for how they relate and react.

Dougherty continues:

Experiments drive the epistemology of science. The product of an experiment is a set of measurements. These form the data of sensibility, the empirical (as opposed to a rational) basis for knowledge. In themselves, measurements do not constitute scientific knowledge. They must be integrated into a conceptual system. Scientific knowledge is constituted via synthesis of the observed measurements. These are related to variables and relations among the variables. A complex of variables and their relations compose a mathematical model. A scientific theory consists of two parts: (1) a mathematical model composed of symbols (variables and relations between the variables), and (2) a set of operational definitions that relate the symbols to data.

The idea of having a conceptual system is critical. For example, when Claude Shannon delivered his theory of information and communication the underlying paradigm was a binary symmetric channel. Namely if I send a 1 the probability of getting a 1 on the receive side is 1-p and the probability of a zero is p. Likewise for sending a zero. Simple, measureable, verifiable, and it became the basis for substantial added complexity without ever having to change the underlying paradigm. Likewise for Newton, F=ma, and we can then add whatever we want to that expression. From Watson and Crick we had; DNA, RNA, Protein. Basically that still works but we now have a lot more baggage.

Dougherty continues:

Scientific truth is pragmatic truth and this truth is contained in the predictive capacity of a scientific theory. Scientific knowledge is about the future. This pragmatism towards the future is bluntly affirmed by Feynman when he writes, "Knowledge is of no real value if all you can tell me is what happened yesterday". Past observations may lead one to construct a theory, say through statistical estimation, but the theory must predict the future. As stated by Riechenbach, "A mere report of relations observed in the past cannot be called knowledge. If knowledge is to reveal objective relations of physical objects, it must include reliable predictions. A radical empiricism, therefore, denies the possibility of knowledge".

Prediction is not certitude. Instead of causality, science involves conditional distributions … Statements concerning conditional prediction can be validated via experimentation. The meaning of a statement can be rigorously defined within the framework of probability theory and its relation to measurable phenomena can be mathematically characterized within the theory of statistics. If the predictor variables are temporally antecedent to the variable to be predicted, then we have forward prediction. The terms "cause" and "effect" never appear because they lack empirical foundation.

Erwin Schroedinger explains, "It can never be decided experimentally whether causality in Nature is 'true' or 'untrue.' The relation of cause and effect, as Hume pointed out long ago, is not something that we find in Nature but is rather a characteristic of the way in which we regard Nature". …

As an illustration, it has been shown that experimentally increasing the levels of the Wnt5a protein secreted by a melanoma cell line via genetic engineering methods directly alters the metastatic competence of that cell as measured by the standard in vitro assays for metastasis. A scientific statement may take the form of predicting the likelihood of metastasis conditioned on the state of the WNT5A gene or the level of the Wnt5a protein. Notice the quantification: there must be a probability of metastasis under some specified set of conditions, and the validity of the statement rests with the accuracy of that probability. It is alright for that probability to be different under different conditions, for instance, depending on the age or sex of the patient, but under each different condition, the validity is determined by the accuracy of the probability statement under that condition. …

Science is not about data fitting….

In fact, the science he speaks of is and only is predictive. But moreover, it must be predictive in a context, a model, of what reality may appear to be based on experimental evidence.

2. SOME BASIC PRINCIPLES

We will develop the design concept in terms of the paradigm developed by Winograd and Flores in their seminal work discussing software development. In the development of a theory for design involving the human user, Winograd and Flores invoke the theories of the German Philosopher, Heidegger. The reason they rely so much on Heidegger is because it was Heidegger who introduced the concept of Dasein, the idea of being as an action, as an ongoing action. Winograd and Flores specifically refer to four key propositions of Heidegger that impact the overall process of modeling. These are:

Our implicit beliefs and assumptions cannot be made explicit.

We all too often may make the statement, "You know what I mean." In so doing we are creating to mistakes. First, the other may never know what we mean just by the nature in which we individually perceive experiences and objects. Second, we may, ourselves, not have the insight to our own true beliefs, because we all too often find ourselves questioning them. Hermeneutics, the study of meaning in documents, has been expanded by Gadamer to investigate human reasoning. Thus, indicates Gadamer, our understandings can change with the time and place. This changing makes the explicit articulation specious at best.

Thus we must be cautious as we develop models. For example we can use pathways but the pathway models must reflect the extent of reality that controls the process. Thus

having a model with just on and off states may be grossly inadequate, we need a model for example which includes concentrations and the details of the kinetics of such reactions.

Practical understanding is more fundamental than detached theoretical understanding.

Heidegger has a concept called "throwness", part of being-in-itself, his Dasein. We know something only by being thrown or involved in it. We know what a radiologist does with an image and how he manipulates it for understanding by doing the process ourselves. We cannot expect the user to detail their beliefs and in fact those understandings are time varying.

For example in pathology, one may first learn cell structure, cell types, different cells, cell aggregation and differentiation. Then say when one must diagnose a prostate cell slide, one expects to see normal glands, normal basal and luminal cells, gland like structures which present as normal. If the glands start to look proliferated, small, and lacking the larger gross structure we may begin to see a malignant change, and if the structure has been obliterated then we see massive malignant change. It takes time to develop that level of expertise, it takes being thrown into many cases, seeing and manipulating many subtle differences.

The case can be ever so more complex say with skin lesions involving the melanocytes. Understanding their change in location, their proliferation, and the interaction and movement are essential to diagnosis.

We do not relate to things primarily through having representations of them.

We relate to things themselves. We do not relate to a representation. The representation to the "thing itself" is done in the context of the task to be accomplished. For example, teleconferencing is useful is we are not to relate to the person but to a subject whose essences can be presented directly through the medium, rather than just a representation. We find that teleconferencing is inadequate for personal contact since the contact is through a representation.

Meaning is fundamentally social and cannot be reduced to the meaning giving activities of individual subjects.

Meaning is obtained in dialog, in a conversational fashion, with the ability to meet consensus. Gadamer and Heidegger both relate meaning to the social process of communicating. Both also relate the evolution of meaning to the ongoing set of discourses. Again it is the Heidegger construct of Dasein that the existing being relates to other existing beings, that the Platonic construct of the ideal may be insufficient and in fact counter-productive.

Specifically, social or conversational activity is the ultimate foundation of intelligibility. This means that both in the design process as well as in the operations process, the need

is critical to have the communications channel be conversational if the intent is to convey intelligibility. If the intent is only to transfer predefined package from one point to the other them the conversationality is not essential. In a multimedia environment, intelligibility in the context of the various media and thus intelligibility demands conversationality.

There is also the issue of “hidden paradigms”, or those shared cultural definitions or examples and “experiments” that allow us to communicate with each other by adding incrementally to that shared base. For example, in developing models for cell dynamics we share the Watson-Crick paradigm, albeit modified. Thus we start there and incrementally “correct” it or incrementally “enhance” it. Yet the paradigm still stands.

We can also try to better understand the interface by recognizing that the challenge is matching man to the machine. To do this we are frequently pressed into a metaphorical set of analogies. Typical is that of "man as the human computer". Metaphors of this type are both powerful explanations of new concepts and clear statements of our total lack of understanding of the issue.

To quote from Mac Cormac:

"Explanations without metaphor would be difficult if not impossible, for in order to describe the unknown, we must resort to concepts that we know and understand, and that is the essence of the metaphor, a juxtaposition of the familiar and the unfamiliar."

MacCormac further quotes from Arbib (see Man a Machine and The Metaphorical Brain);

"We want to understand how people think and behave....In some ways the brain of a man is like the computer of a robot, in others it is akin to the brain of a frog. Our aim here is to convey an understanding of the brain in terms of two main metaphors: The cybernetic metaphor, "Humans are machines," and the evolutionary metaphor, "Humans are animals." We shall downgrade the differences, but we hope to learn much from the similarities."

The harshness of Arbib pronouncements are striking. For indeed he represents the voices of many computer designers who view the human at best as a fellow computer and at worst a level above slime mold. Metaphor is powerful for it is in essence our most gracious way as humans to express our total ignorance of the true essence of the problem at hand.

To use the Heidegger view, the use of metaphor is essential if we have not experienced the throwness of the problem, that we have not immersed our total being in the basic uncertainty at hand. We use metaphors as a way of re-expressing what we already know rather than understanding the unknown.

The danger in the use of such metaphors is clearly that we fail to come to deal with the needs of the end user in interfacing with the multimedia world. We view the end user as another peripheral computer system and not as an entity that must be thrown within the environment to best profit from its performance. Thus, as we saw in the last section, current authors view multimedia as nothing more than another display or another storage device. Their world view, as so aptly developed in Kuhn's thesis, is limited to the existing paradigms. They talk metaphorically as man as computer, or worse as man as frog.

This world view is dramatically different from that of the rational school of thought that focuses on the idea that there exists a perfect truth independent of the individual and that through proper perception as a single individual this truth can be made clear. Heidegger's approach is that we must combine the rational objective world with the totally subjective individualistic world into an environment where the human user becomes part of the environment of the media.

As Gadamer has stated (see Warnke), we understand in a dialog manner. Specifically:

"If one examines Gadamer's analysis ...all knowledge of the natural and social world...is grounded in traditional orientations. We never come upon situations, issues or facts without already placing them within some context...and interpreting them in some fashion."

"In equating the logic of understanding with the structure of dialogue, Gadamer suggests that the proper answer is that ... in genuine conversations ...all participants are led beyond their initial positions towards a consensus..."

Thus the process of consensus in a conversational mode is what leads to new understanding. All initial constructs are based upon prior prejudices that can best be formed in the context of metaphors. If our goal in developing new user interfaces is the ability to allow the users to understand, as viewed by Gadamer, then we must do so as to support the conversational modality and to allow the reaching of consensus.

3. CONSEQUENCES OF HEIDEGGER

Winograd and Flores have noted six effects of accepting the Heidegger world view. These are;

You cannot avoid actions.

Even inaction is a form of action. Managers, as developed by Simon, interact with their day to day industrial environment, and managers who act by inaction have the corresponding results.

You cannot step back and reflect.

Events exogenous to us are continually occurring and any attempt to stop time to best understand the situation is at best specious. At worst, it becomes inaction. The concept of hermeneutics is one that extended to the environment of the end user say that we make interpretation with what is at hand and what is part of our tradition.

Effects of actions cannot be predicted.

We can anticipate, we can plan and we can strategize, but the world is filled with uncertainty. As such, we act in an environment where the exact outcome is uncertain. The user must anticipate that but not be fearful of it.

You do not have a stable representation of the situation.

Every situation is a representation in flux. When a user accesses a system, there are many factors that impinge on the interaction of the user, their needs and responses. No system interface to a user should assume a stable representation of facts. Designs should be such as to prepare for ambiguity.

Every representation is an interpretation.

X rays are inherently representations of physiological factors. In looking at an x ray a physician is looking at a representation and performing an interpretation. When we design a user interface, we are representing a set of facts to the users. The act of the designer in representing the facts is an act of the designer in interpreting for the user the facts. Thus in designing the interface, the designer must be aware of the fact that they are entering into the interpretation process. Not only is the user interpreting but so too is the designer for the user.

Language is action.

Speech through our language is a spontaneous reaction to a set of situations. In the design of computer interfaces we spend many hours on structuring the presentation of the visual material. Images are carefully scrutinized. Speech, in a multimedia context is fluid and open to instant interpretation that may not be consistent with the other participants in the multimedia session. For example, our tone of voice may make us appear arrogant, our questioning may make us appear petulant and our suggestions may make us appear pedantic. Despite all our structured work on the interface, the instantaneous impacts of the language may override the setting. Thus a multimedia environment must have the flexibility to self-correct.

There are eleven design guidelines that Winograd and Flores have articulated and these play well into the end user interface effort associated with multimedia system. These guidelines are as follows;

1. There are no clear problems to be solved. Action needs to be taken in a situation of irresolution.

2. A business is constituted as a network of recurrent conversations.

3. Conversations are linked in a regular pattern of triggering and breakdown

4. On creating tools were designing new conversations and connections.

5. Design includes the generation of new possibilities.

6. Domains are generated by the space of potential breakdown of action.

7. Breakdown is an interpretation - everything exists as interpretation within a background.

8. Domains of anticipation are incomplete.

9. Computers are tools for conducting the network of conversation.

10. Innovations have their own domains of breakdown.

11. Design is always already happening.

If we follow these design rules in developing the human interface and if we understand the underlying theories of human understanding and intercommunication, this will assist the designer in being flexible to converge to a more stable interface.

Language is a means to expresses knowledge. Language is also a means to gain and crate knowledge. We can now expand the concept of a language from what we see as words and what we hear as speech to what we see as actions and what we create as situations. The ability to provide for more breath of language as intercourse and interaction, and the ability to extend that intercourse to all of the senses, no just sight and sound, allows for the attainment of the fulfillment of a multimedia communications environment.

4. DECONSTRUCTION

Deconstruction consists of the unraveling of actions and physical realities to determine the underlying sets of truth, such being definable and determinable. In its simplest state, the unraveling is the determining of intentions within the context of how the intended views the world at the time of the intent. Deconstruction from the perspective of multimedia communications is a toll that helps the designer understand the biases, prejudices and limitations of the designer. Deconstruction allows for the ultimate use of the technology in the context of the user.

We start the development of the deconstructionist approach with the development of the concepts of paradigms and world views. We have already discussed them in some details but it will be critical to the deconstructionist approach to have them developed in full

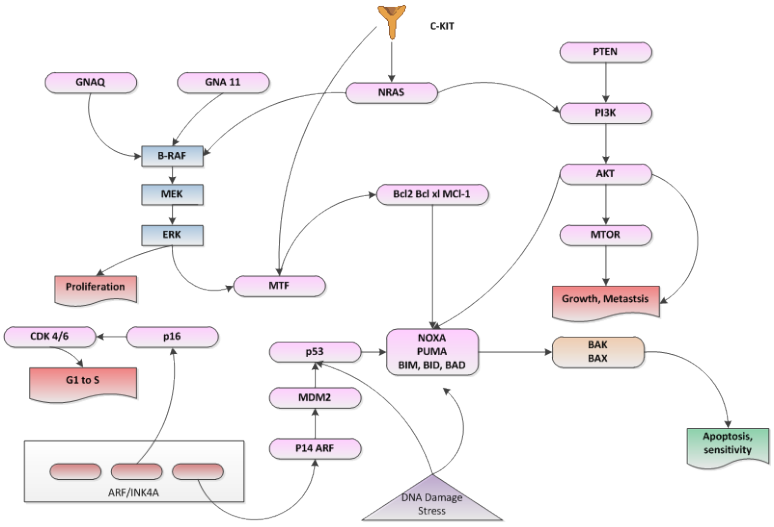
detail. Then we shall move to the analysis of a set of key questions that appear when we begin the development of a multimedia communications theory.

The issues discussed herein can be very critical to how we approach models. Models may very well bring to the table our views of the world, or world view, namely the preconceived notions and prejudices, which result in limitations of what we can achieve in a model. Again as we have discussed in the use of logistic models, they provide a simple way to relate data, but in reality the underlying reality is left aside. That may very well result in non-functional models.

4.1 Paradigms and World Views

The concept of cellular pathway architecture has been a cornerstone in the development of new understandings of disease, disease progression, and disease management. However, the structural elements of these architectures have not been incorporated fully in our studying of disease, and we all too often look solely at genes alone and not as some holistic entity with governing interconnections and a dynamic profile.

Architecture, first, requires that the underlying system be treated in terms of a set of commonly understood elements and that these elements have a clearly demarcated set of functions and interfaces that allow for the combining of the basic set of elements. The way the elements then can be combined, reflected against the ultimate types of services provided, determine the architecture. In our case the elements can be the genes themselves or the products of the genes, namely their related proteins. Further, the proteins may be characterized in terms of concentrations, rather than just their existence or lack thereof. For example we show a typical pathway model below:



The entries may be protein concentrations and the interactions may be defined in terms of reaction kinetic models. This is an expression of the architecture. The elements are proteins, protein concentrations, linkages, reaction kinetics, and possibly several other factors such as activator genes, repressor genes, miRNAs and the like.

Architecture, secondly, is driven by two factors; technology and world view. Technology places bounds on what is achievable, however those bounds are typically well beyond the limits that are self-imposed by the designer or architect in their view of the user in their world. Technology is what we can measure and identify. We can now identify proteins, and in some cases their concentrations. Yet a full model may require a concept of architecture and the use of design elements is critical in understanding the paradigms used in the structure of information systems (SeeWinograd and Flores, pp. 34-50, especially their discussion of Heidegger and Throwness in terms of design). World view is the more powerful driver in architecture (See Kuhn, pp. 72-85). We argue in this paper that it is essential to develop a philosophical perspective and understanding of how to view networks. We argue with Winograd and Flores, and in turn with Heidegger, that we must be thrown into the network, to understand the needs of the users, and to understand the structure of the paradigms that are used to construct the world view.

The concept of a ***paradigm*** is in essence the collection of current elements that we have at hand for the network and the ways we put these elements together. However, the true meaning of a paradigm is in the context of the examples or experiments that we all relate to with that technology. Paradigms are not technology in and of itself, but technology as example. New paradigms result from new technologies. New technologies allow for the placing of the elements together in new ways. Kuhn, then goes on to demonstrate that the world view, that is how we view ourselves and our environment is based upon the our acceptance of these paradigms, as either collections of techniques and technologies or as collections of embodiments of these techniques and technologies in "examples". We then tend to accept this as the way things are and should be. Then Kuhn argues, as the technologies change, changes in the paradigms do not occur in a continuous fashion but almost in quantum leaps. The new paradigms build and congeal until they burst forth with new world views. It is this model that we ague applies to the evolution of broadband.

Thus, ***architecture is the combination of three parts: the common elements, the underlying technology and the world view.*** We depict the conceptualization of architecture as the amalgam of these three elements. We shall develop this construct more fully as we proceed. In cell pathways we have the elements as we have shown above, the technologies are those abilities we have to measure or control the elements, and the world view is how we connect and express the elements as a whole. Thus if we can measure miRNA concentrations via some technology then we include them as an element. Our world view may be looking at a single cell, in contrast to the whole organism.

The concept of a ***world view*** is an overlying concept that goes to the heart of the arguments made in this paper. To better understand what it implies, we further examine several common views and analyze the implications of each. If we view our world as hierarchical, then the network may very well reflect that view. If we further add to that view a bias towards voice communications, these two elements will be reflected in all that we do. The very observations that we make about our environment and the needs of the users will be reflected against that view. As an external observer, we at best can

deconstruct the view and using the abilities of the hermeneutic observer, determine the intent of the builder of the networks.

To better understand the importance of an architecture we develop the concept of the historicity of architectures based upon the work of Kuhn and ten that of McLuhan. Kuhn begins his thesis of how scientific revolutions occur by the introduction of the concept of paradigms. He defines these as (see Kuhn p. 175);

"...the term paradigm is used in two different senses. On the one hand, it stands for the entire constellation of beliefs, values, and techniques, and so on shared by the members of a given community. On the other, it denotes one sort of element in that constellation, the concrete puzzle-solutions which, employed as models or examples, can replace explicit rules as a basis for the remaining puzzles of normal science, The first sense of the term, call it sociological, ..., "

The concept of a paradigm is in essence the collection of current technologies that we have at hand for the network and the ways we put these elements together. Watson and Crick brought forth a new paradigm. New paradigms result from new technologies. New technologies allow for the placing of the elements together in new ways. Kuhn, then goes on to demonstrate that the world view, that is how we view ourselves and our environment is based upon the our acceptance of these paradigms, as either collections of techniques and technologies or as collections of embodiments of these techniques and technologies in "examples". We then end to accept this as the way things are and should be. Then Kuhn argues, as the technologies change, changes in the paradigms do not occur in a continuous fashion but almost in quantum leaps. The new paradigms build and congeal until they burst forth with new world views. It is this model that we ague applies to the evolution of broadband. It is this philosophical view, almost Hegelian in form that is essential in understanding the underlying and formative changes in paradigms that will change our world view.

As a second perspective of the impact of technology as a dominant driver, we can refer to McLuhan and his development of the concept of media. Drucker has referred to the presentation of McLuhan's doctoral thesis and McLuhan is quoted as follows (See Drucker, p. 250):

"Movable type, rather than Petrarch, Copernicus, or Columbus was the creator of the modern world view .... "Did I hear you right," asked one of the professors as McLuhan had finished reading, "that you think printing influenced the courses the universities taught and the role of the university, altogether?" "No, sir, " said McLuhan, "it did not influence; printing determined both, indeed, printing determined henceforth what was going to be considered knowledge."

This concept later evolved into the medium being the message. In our context it is the fact that both Kuhn and McLuhan recognized, albeit in differing fields and in differing ways, that fundamental changes in technology and technique, call it paradigm or the medium, will change the world view, also the message. It is the importance of

understanding the change in the technology, its function and evaluates the possible change that this will have in the world view

Thus, architecture can be defined as the conceptual embodiment of a world view, using the commonly understood set of constructural elements, based upon the available set of technologies.

For example, Gothic architecture was a reflection of the ultimate salvation in God in the afterlife, in a building having a roof, walls, floors, and windows, and made of stone and glass. Romantic architecture was, in contrast, a celebration of man, using the same elements, but some employing a few more building materials. The impact of the differences in world view is self-evident in the embodiments of the architecture. (See the discussions on the impact of world view on architecture in Wolfe. In addition see the cultural or world view impact on the Gothic architectures in Jantzen and in Toy.)

Before continuing, we will define in a more structure fashion the paradigm, the world view, the architecture and the technology base. First, Kuhn defines world view as:[1]

“An entire constellation of beliefs, techniques, and so shared by the members of the community."

And he further defines the paradigm as, first:[2]

"One sort of element in that constellation, the concrete puzzle-solutions which employed as models or examples can replace explicit rules as a basis for the solution of the remaining puzzles of normal science."

And then second as:[3]

“Paradigms are what the members of the scientific community share and conversely a scientific community consists of men who share a paradigm."

We however, take from these definitions and place them into the context that we have developed in this section.

A ***paradigm*** is a unique and defining experiment or demonstration that in and of itself crystallizes a concept as representative and descriptive of a broader class of similar ideas.

The classic paradigm was that of Watson and Crick in developing the structure of the DNA molecule. The defining moment was best described in their paper in Nature that off-handedly alludes to the DNA molecule having the properties of self-replication and

[1]Kuhn (TFTTM, p132)

[2]Kuhn (TFTTM, p175)

[3]Kuhn (TFTTM, p176)

thus containing the genetic information for all life. This defining experiment then led to the massive changes in Botany, Biology, Medicine and even computer science. The paradigm is the rite of initiation for any believer in the new religion. The paradigm for Christianity was the resurrection of Jesus, and that of Judaism was the pact of Abraham with the Lord.

To understand all other elements of deconstructionist thought, it is first necessary to find and identify the defining moment, or the paradigm.

The ***world view*** is the collection of all beliefs that follow from a consistent application of the paradigm in reflecting life and its existence.

The world view of the DNA paradigm is genetic engineering, of the Univac paradigm, is the central processor; of the Church in the Middle Ages is salvation after death. The world view is more than a single statement; it is a collection of beliefs. All the beliefs are predicated on the unique and singular interpretation of the paradigm. Until Martin Luther, the Church in Rome was in control. Luther, through the printing press and the availability of the bible to all challenged and changed this. The new paradigm in this case was the printed bible in vernacular. The world view was that of Protestantism.

All too often we see the world view in parts. Even if we see the world view in total we may fail to see the paradigm. The religious organizations typically define and deify their paradigms. Jesus at the mount, Mohammed and the angel, Joe Smith and the angel, May Baker Eddy and divine revelation, and even the Buddha and his revelations. They are the paradigms. In religion it is critical to have the paradigms unchallenged. They are thus constructed.

The ***technology base*** is defined as the set of all technologies available to demonstrate the paradigm and to implement the representation of the world view.

We define technology in its broadest sense. We may have a paradigm of a god who has shown themselves through the visions of a mushroom. The world view is that we must perform all of our important acts under this influence. The technology allows us to analyze the mushroom and determine based on our neuroscience knowledge that the effects are those of psilocybin, not of our god. That will challenge the paradigm. Another is the ability to measure the age of the earth and to carefully, through genetic analysis, determine the evolutionary pathways of all creatures. This may challenge the paradigm of the creationists. A third, and current one is the technology to determine that homosexuality is genetically based. This challenges the paradigm of choice in the homosexual community and thus attacks a power base. Technology can thus either empower the world view or express it or it can challenge and destroy the paradigm.

Architecture is defined as the conceptual embodiment of a world view, using the commonly understood set of constructural elements, based upon the available set of technologies. When we look at cell dynamics, the models are as much a reflection of our world view as they are a reflection of the reality we are trying to examine.

The ***design*** is the current implementation of an architecture using the current technology base.

The process of ***deconstruction*** is the process whereby the current observer, by using the understanding of the technology base evolution, and by understanding and structuring the current and prior architectures, can determine the base paradigm and thus infer all elements of the world view of the implementer of the architecture.

We shall use this process in the development of many multimedia systems. The design of a multimedia system must understand the paradigms of the users. This is inclusive of all of the user sets, namely the food chain elements that we discussed before. To deconstruct, we must understand and identify the paradigm. Without that we cannot hope to achieve the conversationality that we seek.

Finally, we add the definition of an infrastructure, recapturing what we developed in the last section.

An ***infrastructure*** is a shareable, common, enabling, enduring, resource that has scale in its design, and is sustainable by an existing market, and is the physical embodiment of and underlying architecture.

4.2 Questions

We proceed with the effort of developing a deconstruction theory by developing a set of key questions that ultimately relate to our understanding of object or entities. It will be through this understanding that we come to grasp the underlying structures of multimedia.

4.2.1 1. What is an object?

An object is and entity in a multimedia environment that is actionable. It is a single or compound collection of multimedia elements, combined from one or several users, that creates a transaction. Actionable implies that the objects can be used by others or shared amongst others and the sharing or use results in human actions or responses. The concept of actionable objects is at the heart of multimedia communications.

4.2.2 2. Do Objects exits?

Objects exist through the transactions that they create. Does a conversation exist? Words are created, sounds are made, and a consensus is achieved. Possibly the objects used in the conversations are perceived differently by each of the participants, and possible the consensus is perceived differently, even if it is placed in writing and agreed to by all. The true sign of the objects existing is their ability to create a transaction at some point, namely a change element.

4.2.3 3. What role does the human play in the expression of the characteristics of an object?

Does a tumor such as a lymphoma exist? The patient presents with a symptom of a swelling in the neck. The physician palpates and remembers the past 99% of the cases were lymphomas, by definition; the pathologist reads the slide and sees the telltale cell pathologies. The object of the lymphoma exists. The existence is in the consensus of the individuals. The ultimate existence is in the life or death of the patient

4.2.4 4. How does a human deal with objects?

The human deals with the set of objects through their totality of senses. The object may be visual, all too frequently what we are trained to respond to in today's culture, it may be a sound, a touch, a smell, or any of the other sensual combinations. The human rationalizes the sense objects and creates a communal sense of agreement with others with regard to a collection of such objects. The human deals with multimedia communications objects in a conversational and communal fashion. Unlike a book, or a video game, which is an internalized experience, a multimedia communications based object is externalizable, and allows for the displaced conversationality described earlier.

4.2.5 5. Why does a human deal with an object?

The human deals with the objects through their senses and with the interaction of other humans. It is a consensus-conflict resolution process.

4.2.5.1 6. Why does a human react to the presence of an object?

The human reacts to the object by transacting an event. The multimedia objects are essentially demands on the individual’s senses that will not go unanswered. It is an active medium that demands a reaction and response. Unlike television which may be internalized and has responses that are displaced in their cultural context, multimedia communications is in the context of a real time communal dialog.

4.2.6 7. "What is communications?"

Communications in the context of multimedia is a conversational transaction. It allows multiple individuals, humans or otherwise to interact, converse, and through that conversation to transact. Communications is the movement of information between individuals, movement that entails the interaction of as many of the sense as is possible.

4.2.7 8. "What is conversation?"

Conversation is the sharing of senses, the establishment of consensus or the resolution of conflict, with the end result is the transaction. A conversation requires two or more humans, a common shared medium, contemporaneous or otherwise, and a shared set of beliefs that allow for a common understanding of the signs used on the conversation. The semiotician would look at the conversation in terms of the external signs. The deconstructionist would look at the underlying pre-beliefs of the communications. The hermeneuticist would try to understand the motives of the messengers in the conversation. In the case of multimedia communications we are using signs that are externalities of ideas that we wish to transmit from one individual to another. The end result of this transmission of ideas is a transaction, a change in the state of the receiver or even the sender of the ideas.

Multimedia communications is about conversations. It is about using all of the constructs available to communicate information that results in that desired or otherwise transaction. The challenge is to determine what elements are necessary for the state change. The further challenge is to determine if that change really occurred.

4.2.8 9. "How do humans interact with information?"

Humans interact with information by responding and creating a transaction. Information allows the change of knowledge state in the individual. If I am provided with a new piece of information, I change my understanding of something that I had not fully understood before. It may clarify it or it may dramatically alter it. If there is no change, then we argue that there was no information.

4.2.9 10. "What is a representation?"

A representation is an embodiment of a collection of information elements. In a multimedia communications environment we are almost always dealing with representations and never the actual entity. For example, in a radiological environment, we look at the MRI of the brain of a patient with multiple sclerosis. We see in the brain the white spots that represent the demyelination of the brain cells, the evidence that there is a sclerotic event. If we were the surgeon, we would most likely see nothing, if the pathologist, we would see the demyelination on a different scale by staining the cells and see the loss of myelin. All are representations of the underlying disease process. The reality so as best defined a genetic and viral induced process that is the human’s immune system rejecting the self. This is the long winded way of defining the entity via the process as compared to defining the entity via the representation. The representation defines an entity that may be defined in no other way.

4.2.10 11. "Does there exist an abstraction that can be shared by two people that allows common understanding?"

The essence of multimedia communications is the delivery of abstractions. An abstraction is a representation of an entity delimited by the technological resources available in the multimedia communications environment. A full representation may require all the senses, or a breath of the senses that exceeds what is generally available to the current technology. The abstraction is the mapping of the representation onto the technology base. Sharing abstractions may allow two or more people to attain a common understanding if there is adequate information conveyed in the abstraction. For example, two physicians may see a chest x ray and determine that the patient has a carcinoma of the left lung. The spot is clear and non-disseminated, and based upon mutual shared prior experience it is clear what the abstraction is saying. If one of the viewers is the patient who is not medically trained, the abstraction would not convey such information. Thus information exchange requires a shared abstraction as well as a shared experience base with that set of abstractions. Expecting that abstractions per se convey information is not viable. However abstraction become short hand notation for what lies behind them.

4.2.11 12. "Does a representation exist independent of the observer?"

This is the dualism between forma and substance, between essence and existence. Is there such a thing as a rose, or is there a set of observable that when clustered together reach the consensus in most people that this is a rose. The body of plant Systematics faces this problem at all times. The answer is that there is no such thing as an abstract representation. Information and determination, the transaction, take place with a set of noisy observations that have been characterized and categorized.

4.2.12 13. "Does a representation change in its meaning when observed by more than one observer?"

This is the same as asking if consensus changes if there are more or less participants in the process. Will a jury meet a different decision if there are different jurors? The answer is possibly. Consensus is convergent but there is no abstract convergent point.

Why are these questions important and how do they relate to multimedia communications. Multimedia communications consists of communicating objects that relate to the human in only one fashion; through a transaction or through the empowerment to act. When designing a system, we empower the users to act. They must do so through the use of objects, the manipulation of the objects and the gaining of a consensus.

4.2.13 Answers?

The questions posed in the last section and the discussion concerning them clearly indicate that a certain set of long standing issues are still at the heart at how we view ourselves as creatures. The main driving issue has been the mid and body dualism. As we creatures that think with and act with our minds, or are our bodies the totality of ourselves. To quote from Winograd and Flores:[4]

[4]Winograd & Flores (UCC p 30-31)

"...mind-body dualism...rests on several taken-for-granted assumptions:

1. We are inhabitants of a real world made up of objects bearing properties. Our actions take place in that world.

2. There are objective facts about the world that do not depend on the interpretation or even presence of any person.

3. Perception is a process by which facts about the world are registered in our thoughts and feelings.

4. Thoughts and intentions about action can somehow cause physical motion of our bodies."

This concept of the ideal form and the ideal an achievable entity is as old as Plato and Aristotle. The concept of the ideal form, as a Platonist would state, is that there is a true idea of a daylily. It is an abstraction that is the daylily, and what we see as humans is a mere shadow of its true form. To the multimedia communications, we then ask how does a Platonist communicate, namely, does he try to use the abstraction that closely matches the form? Copleston speaks on this with regard to Plato:[5]

“I would point out that the essence of Plato's doctrine of Forms and Ideas is simply this: that the universal concept is not an abstract form devoid of objective content or references, but that to each true universal concept there corresponds an objective reality."

Continuing he states further:[6]

"In the Republic it is assumed that whatever a plurality of individuals have a common name, they have also a corresponding idea of form. This is the universal, the common nature or quality which is grasped in the concept."

It is the attempt to describe the "nature" or essence of things and to use this as a means to communicate that is the basis of many of our problems in design. An example is the compression of speech or video. We compress to avoid the need for more bandwidth. We compress also because we believe that by doing so we get to the essence of it. We do so in a Shannoesque fashion, assuming that there is an essence of bits, minimal as they may be. This extension is best described by Popper:[7]

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[5]Copleston (Vol I, Part I, p. 175):

[6]Copleston (Vol I, Part I, p. 175):

[7]Karl Popper has stated (Hull, Ershefsky ED. p 201):

“I use the name methodological essentialism to characterize the view, held by Plato and many of his followers, that the task of pure knowledge or "science" to discover and to describe the true nature of things; their hidden reality or essence. ...All these methodological essentialists also agreed with Plato in holding that these essences may be discovered and discerned with the help of intellectual intuition. A description of the essence of the thing they called the "essence"."

An extreme position to this essence approach is the positivist approach expressed by Ayer when describing the early work of Wittgenstein.[8]

"..the main theses of the Tractutus can be easily summarized. The world is said to be totally of facts which themselves consist in the existence of what are called... atomic facts... or states of affairs. The states of affairs consist of simple objects, each of which can be named. The names can be significantly combined in ways that express elementary propositions. Each proposition is logically independent of all its fellows. They are all positive and each of them depicts a possible state of affair which constitutes its sense....The fact that they are logically independent means that in order to give a complete account of reality one has to say which of them is true or false."

The development of multimedia is the development of new metaphors. MacCormac best describes this change that metaphor can take:[9]

“Metaphor can be described as a process in two senses: (1) as a cognitive process by which new concepts are expressed and suggested, and (2) as a cultural process by which language itself changes...epiphors are metaphors that express more than they suggest… diaphors suggest more than they express."

He goes on to state:[10]

"Generations of students who have passed through introductory philosophy courses in colleges and universities have come to believe in the division between the mind and nature. The rise of cognitive psychology in opposition to behaviorism, which denied the existence of the mind, fins comfort in the philosophical efforts to build a foundation for knowledge. The account that I have presented of metaphor as a cognitive process presumes the existence of the mind existing as a deeper level of explanation that of semantics and surface language."

The essence of the Heidegger philosophy as relates to multimedia design has been best described by Winograd and Flores:[11]

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[8] Ayer(Witt, p 17)

[9] Mac Cormac (Met, p 5)

[10] Mac Cormac (Met, p 155)

[11] Winograd & Flores (UCC p 30-31)

"We...present...a...discussion of Heidegger's philosophy,

(1) Our implicit beliefs and assumptions cannot be all made explicit.

(2) Practical understanding is more fundamental than detached theoretical understanding.

(3) We do not relate to things primarily through having representations of them.

(4) Meaning is fundamentally social and cannot be reduced to the meaning-giving activity of individual subjects."

The final element of Heidegger's approach is the breaking down effort of providing information in a way in which it is broken down or handled by the user.[12]

"... Heidegger's ...insistence that objects and properties are not inherent in the world, but arise only in an event of breaking-down in which they become present-at-hand...In sum, Heidegger insists that it is meaningless to talk about the existence of objects and their properties in the absence of concernful activity with its potential for breaking-down."

The latter comment on Heidegger is the essence of multimedia communications. The breaking down if the basis of a transaction, of a change in state of the human or humans in the conversation. We must then take into account the impact of this new medium. It is an impact with many dimensions of consequences.

To quote McLuhan:[13]

"The personal and social consequences of any new medium result from the new scale that is introduced into our affairs by each extension of ourselves or by any new technology."

And to further the quote:[14]

"The message of any medium or technology is the change of scale or pace or pattern that it introduces with human affairs."

The multimedia revolution is on the scale of all other revolutions. It will be a revolution if and only if it does to the multimedia word what the printing press did to the written word. To quote McLuhan:[15]

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[12]Winograd & Flores (UCC p 36-37)

[13]McLuhan (MIM, p 23)

[14]McLuhan (MIM, p 24)

[15]McLuhan (MIM, p 29)

"The French Revolution, as per de Tocqueville, was a result of the homogenizing nature of the printed word."

Homogenizing means making it accessible to all. Making it accessible means making it actionable, and actionable at a distance. The actionable at a distance, and the ability to have the throwness in the medium and the integration with the message is what will make for the revolution.

5. HERMENEUTICS

Deconstruction is the process whereby the current reader attempts to place themselves in the context of the writer, both used in generic terms, and determine what the message was that was meant to be sent, relative to the context of it being sent. It in many ways is a Bayesian analysis of a human communications process. Hermeneutics is complementary to this effort. Hermeneutics, named after the god Hermes, is in essence the attempt to understand the environment of the singer and writer of the songs, but to sing them as clearly and faithfully as one can. [16]

5.1 Hermeneutic Principles

Hermeneutics is originally imbedded in the interpretation of texts. In our analysis the "text" is the broadened entity of the multimedia environment. The "text" must be expended into the context of the Messenger as carrier of the Message. Thus the need for a hermeneutic understanding is to focus on the messenger and what does the messenger bring to us about the message. In very practical terms, therefore, the same hermeneutic arguments that allowed us to address how to interpret the bible, are and will be at the heart of how do we interpret an x-ray and blood smear in a multimedia environment. The question posed is that does the multimedia environment land through the changed medium ad different message since it is communicated by a different messenger. Or, do we try to ensure that he messenger is kept intact. Another analogy is does the bible change when one understands it from televangelists rather than reading it. Or historically, does the bible change when each person reads it as compared to having it preached from the pulpit. The latter change led to the reformation and the end of the hegemony of Catholicism in Europe.

The hermeneutical school is a contrast to the positivists who argue that one can obtain objective knowledge. To the hermeneutic student, all knowledge is "interpretation".[17] It is in this noisy channel that we try to obtain information. It is thus upon this noisy information that we ultimately act. The multimedia architect must take this into account in the designs of their systems. The channel is inaccurate and furthermore the messenger

[16] Illich & Sanders (ABC, p 85): "The early Greeks had a sporting attitude towards duplicity..."untruth" is always the telling of things that are not, not of thoughts that are contradicted. The patron of this cunning craft was Hermes, the trickster, the thief and the inventor of the Lyre that urges the singer further into epos."

[17] See Warnke, p. 1.

may actually be devious. The theory of hermeneutics attempts to address the issue of devious messengers in the context of texts. We argue that the same questions and approaches are essential for the development of "multimedia text" messages.

The issue relating to texts is developed in Warnke. She states the problem in a historical context:[18]

"Questions of interpretation had been raised earlier, in particular in the Reformations Challenge to the catholic reign of the bible. Did an understanding of Scripture require a prior acceptance of the precepts of the Catholic faith or could it be understood on its own?...Schleiermacher significantly expanded the scope(asking) how many could be comprehended, what methods would permit an objective understandings of texts and utterances of any kind...Dilthey even asked broader questions: what were the methods that would permit an objective reading of any kind, including actions, social practices, norms and values? How could the understanding of meaning be raised to the same methodological clarity characterized in the natural sciences? How could it find as solid a basis for methodological progress?"

Gadamer is the most recent and articulate espouser of the hermeneutic school. He has evolved and matured the hermeneutic approach from one of literal translation to exposition. To quote Warnke describing the evolution in hermeneutics in Gadamer;

"The Bible is assumed to have a normative authority for everyone and the task of the hermeneutic understanding is therefore simply to help transmit the content of its normative claims." [19]

Simply put, Hermeneutic in this context states that the deconstructionist approach may be used in a relative setting, but in the context of a normative setting such as the law of God, we us either hermeneutic approach to seek the "truth" or normative facts. The difference is best stated in terms of selecting a justice of the Supreme Court. Judge Bork is the classic hermeneutic seeking the letter of the constitution. Justice Douglas is the deconstructionist trying to take Madison's words and placing them in a current time frame.

Gadamer takes the hermeneutic goal of positivism and objective answers and introduces the subjective. This is characterized again by Warnke:[20]

"Hermeneutics, as Gadamer conceives of it, then, is no longer to be seen as a discourse on methods of the "objective" understanding as it was for the hermeneutic tradition of Schleirmacher and Dilthey. It no longer seeks to formulate a set of interpretative rules; rather, in referring to his analysis as "philosophical hermeneutics", Gadamer turns to an

[18] Warnke, pp. 1-2.

[19] Warnke, p. 9.

[20] Warnke, p. 3.

account of the possibility of understanding in general, conditions that in his view undermine faith in the ideas of both method and objectivity. Understanding is therefore rooted in prejudice and the way in which we understand it is thoroughly conditioned by the past of by what Gadamer calls "effective history"."

From our perspective, as designers of multimedia systems, we have a cultural environment that we are working in. We have an environment with a history, a past, a culture, and a noisiness that makes event objective transmission of information a transformation of information. The hermeneutic channel challenge is to model the channel, to deconstruct its structure, to generate the optimal processing filters for the complex messages that are to be transmitted.

From a historical perspective, the hermeneutic problem for the multimedia designer is the same as the random noise problem was for the designer of signal detection systems of the 1940's and 1950's. As we had indicated before, it was the work of Shannon who determined that information was essential the elimination of uncertainty. Shannon's teacher, and in many ways mentor, was Norbert Wiener. It was to Wiener, who had both mathematical and philosophical raining, that the development of the concepts of the detection of signals in noise is credited. Wiener conceived of the use of the correlation and auto correlation functions. He introduced the history of an random process in a structured for that has led to information theory and the processing of signals in computers and communications. It is the same construct that we are trying to develop that is of utmost importance. The mathematical theory may not be in place, but the philosophical constructs to develop them must first be worked through.

Warnke goes on in terms of hermeneutic development:[21]

"Hermeneutics thus has a largely pedagogical task: it is supposed to exhibit the truth that inheres in a given claim so that its audience can understand and learn from it. As hermeneutics develops, however, attention is redirected from the understanding of truth context of a text and towards the understanding of the intentions. The aim of understanding is no longer seen as knowledge of die Sache- *a substantive knowledge of claims to truth or normative authority. It is seen rather as insight into the historical and biographical circumstances behind their expression. Understanding becomes genetic: what were the conditions under which the agents acted, spoke or wrote as they did?"*

This leads to a focus on the circumstances qua written word. Deconstruction focuses on the meaning qua circumstances. We must enter into the hermeneutic thought process from the perspective of multimedia communications because the displacements of Gadamer and Habermas are physical and temporal, but the displacements of multimedia communications are electronic and cultural. The nature of displaced understanding is the same in both cases. The issues, we argue, are also isomorphic.

[21] Warnke, pp. 9-10.

The complementarity of approaches can be related to the complementarity of ideas in cultural context. For example, Bloom recounts the issue in the context of the French;[22]

" Descartes and Pascal are national authors, and they tell the French people what their alternatives are, and afford a peculiar and powerful perspective on life's perennial problems...On my last trip to France I heard a waiter call one of his fellow waiters a "Cartesian"...Descartes and Pascal represent a choice between reason and revelation, science and piety."

These two authors are also choices between two types of certainty; the divine and the mind. In reality, as we have seen with Gadamer, certainty of any kind has its limits. The positivist school still argues for the existence of absolute certainty. The hermeneutic school of Gadamer eschews such certainty. At best we can interpret. At worst, the interpretation is a reflection of our own past, history, biases and intents. Even in medicine, the process of diagnosis is one of noisy interpretation. Certainty may exist in a pathology slide that portrays without doubt a malignancy. The outcome of that diagnosis may still have some uncertainty.

Namely, there is a philosophical underpinning in our general line of communications. It is this basis that will lead to understanding or cacophony. Gadamer goes on to define his focus in hermeneutics as follows;[23]

" The task of philosophical hermeneutics, therefore, is ontological rather than methodological. It seeks to throw light on the fundamental conditions that underlie the phenomenon of understanding in all of its modes."

Gadamer further stresses the importance of language in this process:[24]

" Language is the fundamental mode of operation of our being-in-the-world and the all-embracing form of the constitution of the world."

The issue of language being the form of history, the carrier of the formation, and the medium of the message, and thus being the message itself, has implications to the hermeneuticist. One of these is the change in the nature of the media for the transmission of the e message. Weizenbaum notes:[25]

" The computer has thus begun to be an instrument for the destruction of history. For when a society "legitimates" only those data that are "in the standard format" and "that

[22]Bloom (CAM, pp 52-53).

[23]Gadamer (Phil Herm, p. ix)

[24]Gadamer (Phil Herm, p. 3)

[25]Weizenbaum (CP&HR, p 238)

can easily told to the machine" then history, memory itself, is annihilated. The New York Times has already begun to build a database of current events...from which historians will make inferences as to what really happened."

The conversion of words in the twelfth century, with the rediscover of the Greeks and their thoughts, which arguable led to the enlightenment of the twelfth century itself, was a result of the translation, and not simple transliteration of the Greek texts. As Illich and Sanders remark:[26]

" The Greek work was not to be turned into Latin verbum pro verbo. Instead, the meaning was to be detached from the words of one language and made to reappear in another; content, stripped of its form, was to be preserved. Theories about translation changed very little - translation was described as an attempt to divulge the secrets of one language into another- until the hermeneutics of the 1950s. Only then did the study of translation as applied linguistic theory become separated from literary theory."

Ironically, the twelfth century Latin of the early universities, such as those in Paris, was a Latin ready for the expansion of the new technology of Guttenberg. It was now a language whose form was prepared for text. Again Illich and Sanders remark;[27]

" Division into words first came into common use in the seventh century. It happened at the northern frontiers of the known world, where Celtic "ignoramuses" had to prepare for the priesthood and needed to be taught Latin. Division of words was thus introduced as a means of teaching Latin to barbarians as a foreign language."

The very structure of language had made a transition into a form that would allow it to be further tempered by a technology and thus be transformed into the new medium. The bilateral change of the understanding of the environment of the author and the tempering of the environment of the reader then leads to the full hermeneutic context. As Winograd and Flores remark:[28]

" .. Gadamer takes the act of interpretation as primary, understanding it as an interaction between horizon provided by the text and the horizon that the interpreter brings to it. Gadamer insists that every reading or hearing of a text constitutes an act of giving meaning to it through interpretation."

Thus the hermeneutics of Gadamer is evolutionary from the revelation of the underlying eternal truth, to the evolving interpretation.

5.2 Hermeneutic Methodology Applied

[26]:Illich & Sanders (ABC, p 54)

[27]Illich & Sanders (ABC, p 46)

[28]Winograd & Flores (UCC, p 28)

In this section we take the philosophical theory developed in the prior section and address it to the problems of the multimedia methodology. We develop the design principles in hermeneutic observations. The process is to state the observation and then to reflect on the appropriate design principle.[29]

- *What we observe is a reflection of what is there filtered through the understanding of what we think should be there.*

- *Conversations have history, and the history is often unknown, and if known may not be aware to the conversant.*

- *Absolute "truth" does not necessarily exist in a conversation. Consensus may converge but convergence is not to truth. The convergence of consensus is not consistent.*

- *Tradition, authority, and history are integral elements in filtering understanding. The issue of authority is an integration of visions of the presenter and the information presented. Choice of words and language to create a "text" is the basis of power in the relationship.*

  Communications is a sociological interpretive process that seeks to attain consensus in resolving an ambiguity. Actions are the result of that consensus becoming an agreed to common state amongst the community in the process.

6. SEMIOTICS

The theory of semiotics is the theory of signs.[30] Umberto Eco, academician, leader in the field of semiotics, and author, has written several novels, one being the "Sign of the Rose". The novel is about the fourteenth century and about a murder in a monastery. The hero uses the signs that are left behind, the clues in common parlance, to play two roles. The first is the common role of the clues to the murder mystery and the second as the signs to the change of the old guard to the new. It is at the steps of the Renaissance and the signs of most importance are the books of old knowledge. Thus Eco combines all elements of the deconstructionist, with those of the hermeneuticist and those of the semioticist.

6.1 A Definition

Eco defines semiosis as;[31]

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[29]The reader should note that these principles are those of the author as a condensation of the hermeneutic understandings presented in the prior section. The reader may themselves question each of the observations, and that process itself is critical to the design process. The focus is on the philosophical underpinnings of design, and then design as a result of that process. In effect it is essential to perform other acts.

[30]The Greek word semeion, is the word for sign; see De Saussure, p. 147, Taylor, Ed., Deconstruction in Context.

[31]Eco (Semi, p316)

“Semiosis is the process by which empirical subjects communicate, communications processes being made possible by the organization of significant systems. Empirical subjects, from a semiotic point of view, can only be defined and isolated as manifestations of this double (systematic and processual) aspect of semiosis. ...Semiotics treats subjects of semiosic acts in the same way: either they can be defined in terms of semiotic structures or-from this point of view- they do not exist at all."

The elements of semiosis comprise signals and signs. These Eco defines as:[32]

“We are now in a position to recognize the difference between a signal and a sign...as sign may be an expression system ordered to content, but could also be a physical system without any...purpose. A signal can be a stimulus that does not mean anything...a sign is always an element of an expression plane... correlated to elements of a content plane."

Specifically, Eco combines these as:[33]

"Semiotics is mainly concerned with signs as social forces."

Semiosis is based upon the extension of Pierces concept of pragmatism. The Pierce view of pragmatism is presented by Copleston;[34]

“Pragmatism, as Pierce conceives it, is a method of reflection having for its purpose to render ideas clear. ... Pierce divides logic into three main parts, the first of which is speculative grammar...concerned with the ...meaningfulness of signs. A sign...stands for an object to someone whom it arouses a more developed sign. The relation of significance, or the semiotic function of signs, is for Pierce...a relation between sign, object and interpretant."

The issue of semiosis as a carrier of information is also embedded in the issue of a code. Eco defines this as follows:[35]

"..A code establishes the correlation of an expression plane with a content plane...a sign-function establishes the correlation of an abstract element of the expression system with an abstract element of the content system...a code establishes general types... producing the rule which generates concrete tokens...both ...represent ...the semiotic correlation and with which semiotics is not concerned.."

The most descriptive distinction of what semiosis does in comparison to hermeneutics is best described by Eco:[36]

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[32] Eco (Semi, p 48)

[33] Eco (Semi, p 65)

[34] Copleston (HOP, 8-II p65)

[35] Eco (Sem, p 50)

"In order to understand the history of Christian theology, it is not necessary to know whether a specific actual phenomenon corresponds to the word, transubstantiation, it is necessary to know what cultural unit ... corresponds to the content of that word.

The semiotic object of semantics is the content, not the referent, and the content has to be defined as a cultural unit..."

The totality of semiosis is its ability to combine its constructs with all elements of signals and signs. [37]

"...semiotics has been provided with a paramount subject matter, semiosis. Semiosis is the process by which empirical subjects communicate, communications processes being made possible by the organization of significant systems. Empirical subjects, from a semiotic point of view, can only be defined and isolated as manifestations of this double... aspect of semiosis. ... Semiotics treats subjects of semiosic acts...either they can be defined in terms of semiotic structures of-- from this point of view -- they do not exist at all."

Eco has demonstrated the semiotic content in many disciplines. The following table is a summary of these results.[38]

We can now develop some of the basis theory of semiotics as presented by Eco. We start with a set of definitions and then discuss some of the implications.

Expression Plane: This is the plane of understanding in which one creates meaning through and abstract expression. In physics, for example the expression plane may state the following:

$$\frac{\partial^2 E(x,t)}{\partial^2 t} = \frac{1}{c^2}\nabla^2 E(x,t)$$

This expression is the expression for the propagate of light or any other electromagnetic wave in free space. Another example is the composition of a gene;

{ATTGTAAGCCGGATTTTC}

This is a set of nucleotides that imply their complements on the opposite side of the DNA pair. This sequence means a great deal to a molecular biologist. They may imply blue eyes, green wings, or red flowers. Both of these items are in the expression plane.

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[36] Eco (Sem p 62)

[37] Eco (Sem p 316)

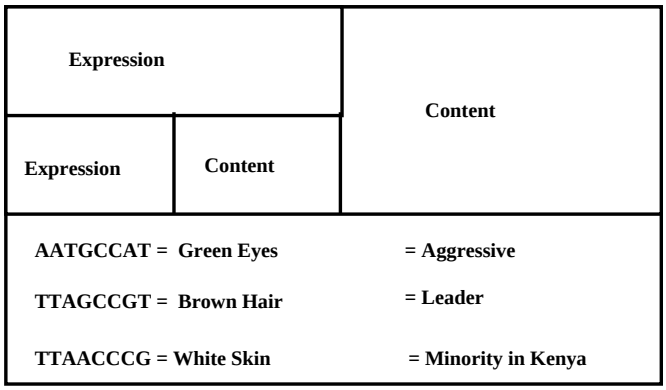
[38] Eco, pp. 9-14

Content Plane: The plane in which one creates meaning through concrete expressions expressed in a continuum of actions in the physical world. Simply put, it is everything that you can think about it...

Let us take the propagation equation. This may be the expression of a rainbow. The content plane is the rainbow and the full panoply of what it evokes. It is macro and micro in its expression. It is the emotion that it may evoke leading to poetry, the grandeur it mat evoke in nature and whatever else may do.

In the genetic case it is the fullness of the expression of the gene and its characteristics. It is the expression of what green eyes may have and the human emotions that they may evoke.

Connotative Relationships: A concatenation of the E/C plane such as shown below;



This example demonstrates the concatenation possible between the Expression and the Content and how content may be concatenated upward itself. Eco makes this example one step further when he states:[39]

"Semiotics is mainly concerned with signs as social forces"

6.2 Semiotic Application

As we have defined the semiotic approach it deals with the signs or externalities of the process of communications. In the multimedia world these externalities are the elements themselves, the data objects, the storage objects and the actual human interaction with devices. All are signs.

Signs are means by which we relate from one plane upward to another. Signs in the multimedia world focus on relating from the image and the test and the voice segment to the determination of the diseased state. The design problem for the multimedia semiotician then is to go from expression to content. The design problem for the semiotic architect is the opposite; from the content to the expression plane. How, does the semiotic

[39] Eco, p. 65.

multimedia architect ask, does one ensure that the expression of the multimedia system contain adequate elements to reflect the process in reverse and ensure the commonalty of expression by the richness of the expressionist?

7. THE THEORY APPLIED

The book, *Epistemology of the Cell*, by Dougherty and Bittner is a gem. Dougherty is a Professor at Texas A&M and has written extensively and brilliantly on the issue of using systems thinking in the growing field of genomics. Now "systems thinking" was, in way, started by Norbert Wiener in the 1930s, as he began to model various systems, from the dynamics of nerve fibers to the development of the first artificial arm. Yes, he did the arm, not the physician at Mass General. Wiener also developed the systems to the control the pointing of radar controlled guns on ships in WW II.

What made Wiener unique was that Wiener asked "Why". The why meant finding the cause and the result and establishing the connection between the two, establishing the system? Physicists and chemists ask "why" questions, the find the cause and the causality chain. Biologists were for ages asking "what" as people who classified. Darwin broke that chain of biologists somewhat by asking "why" as regards to evolutions and he is pilloried even to this day. Physicians often ask "what" and "how" and do not really want to be bothered by the "why". It is not their jobs to find out why, just find out "what" is wrong and know "how" to fix it. Thus a physician is taught "what" to look for to diagnose prostate cancer and is also taught "how" to remove it. The physician does not know or care "why" the cancer is doing what it is doing. That is epistemological.

That in essence is a simplification of what Dougherty and Bitter go about to explain. Their book explores the challenges set forth to those exploring the gene and the cell and entices them to think beyond just the "what and how" to go to the why, the explanation of the process, the system, from cause to effect. The authors have written a treatise which compares a few others which look at the epistemological basis of research, asking the correct questions, and pursuing the best path to answer them (see Winograd and Flores as a prime example written some 25 years ago). Dougherty has with his colleagues and associate been developing the ideas contained herein for well over the past decade and I have read many of his works, they provide great insight to what should be done.

Chapter 1 begins with a discussion of the definition of epistemology, on p. 2. They define scientific epistemology by what it addresses; knowledge and its truth. Then they use Kant to develop the transition from the Enlightenment to today. On p. 4 there is a brief but focusing discussion where he explains the simple Newtonian world maturing into an Einstein one and likewise a Watson and Crick paradigm of DNA/RNA/proteins into the way we understand cell dynamics today, as pathways, miRNAs, repressor enzymes and the complexity of both intracellular dynamics and intercellular dynamics. They rely extensively on a Popperian view of Science, which for those more familiar with Kuhn may tend to have some slight dissonance, but it holds together quite well.

All in all, Chapter 1 sets the stage well, both from establishing the necessity to have models which answer why, and to establish the counterpoint of the thinkers who have reverted back to Aristotelian classification as the finders of what.

Chapter 2 is a discussion of Aristotelian causality. p 14 states it well with the statement, "*explanation must involve a causal relation…*"

On p 21 they state, *"Galileo and Newton do not deny causality as a category of knowledge but they widen the scope of knowledge to include mathematical systems that relate phenomena, while bracketing "questions about nature" of the phenomenon…"*

On pp 33-34 they have an excellent discussion of Bertrand Russell's work on causality.

In Chapter 4, on p 70, the authors use the work of Norbert Wiener and his associate Arturo Rosenbluth on Cybernetics. For it was indeed *"the synergy of communications, control, and statistical mechanics…"* that set the framework of how we should view cellular and organ dynamics. The authors then gave examples of gene regulation. I would have simply stated that every cell and every organic system is a multidimensional distributed random process.

One could take a Feynman like approach and posit the obvious, and then fill in the details. The authors work from the bottom up to demonstrate their world view. Namely that when we look at cells we are looking at complex dynamic random systems. Systems we can ascribe states to, states being measurable quantities, which in turn operate on other states in a dynamic fashion.

In Chapter 5 the authors start the transition to complex state models. They again rely on the wisdom of Wiener on p 89 to state:

"Wiener recognized the difficulties that the mathematical requirement of science and translational science would present for medicine …"

For back in 1948 when Wiener had published Cybernetics, Medicine was still a "*what and how*" practice. It did not transition to a "why" approach. The translational science that the authors speak of is:

"… mathematical engineering, applied mathematics with a translational purpose..."

Namely, to translate nature to measurable quantities. Quantities which we can then by knowing the "system" we can then manipulate and predict. We can observe and we can control the end goals of translational science. In a Popperian sense, the authors address the issue of measuring, predicting, and examining what does not do what we said it would.

The key arguments are developed in Chapter 9 and 10. Chapter 9 is the "sola fides" discussion, *faith alone,* as a mantra to those who fail to understand the system nature of

the cell dynamics. The authors, on p 149, evoke William Barrett, the insightful Columbia University philosopher, who wrote *The Illusion of Technique*, a superb work integrating the principles of epistemology and science in the late 1970s. Frankly, to see Barrett in a book of this type was an exciting surprise, for I had thought that Barrett was falling into obscurity, a loss to many who are struggling with issues that Barrett has thought through decades ago. The authors then on p 148 also discuss the nature of stochastic dynamic systems.

Dougherty brings insight via avenues that I found resonated strongly. The discussion on Wiener, where Dougherty, unlike Gleick in what I feel is presented with uninformed bias, sees Wiener as the father figure, one combining systems thinking, clear and built upon strong mathematical foundations, which is then integrated with real biological systems. Although I find their approach insightful and compelling, I would have taken pathways in cancer dynamics as somewhat well-defined stochastic systems.

For example, we know the effects of PTEN, the AKT pathway, and the MYC pathway, the p53 pathway, and the complex dynamics which are well described in the readily available NCI data base of pathways. One can use as states the concentrations of any one of these proteins and then state simply that they all interact with one another, the result being homeostasis or if a change cancer. The model is multidimensional, stochastic, highly complex, and strewn with “noise”, namely uncertainties. Models have been developed and tested for such cancers as prostate, melanoma and colon. Dougherty, himself, has made substantial contributions to this area. It would have been useful perhaps to demonstrate this approach as well.

On p. 163 the authors place a stake in the ground to say what would be expected for those to work in the field, that the books by Loeve and Cramer be used as standard bearers! As I read that in the book I looked on my bookcases and saw my old well-worn copy of Loeve, which got me through my PhD. Cramer was my core text for my introductory course, but then again it was MIT. Thus they set a high hurdle, but a necessary one for those to work in the field. My first book, *Stochastic Systems and State Estimation* (Wiley, 1972), in a sense was one of the many which established the bar.

The clear strike at the adversaries is set on p. 165. After again referring to Barrett and Kant, the authors end with:

“Does anyone really believe that data mining could produce the general theory of relativity?”

I think this can be extended. For example many researchers run millions of microarrays and are currently finding hundreds of SNPs or thousands of miRNAs and each time they send out a press release saying they have “discovered” some new “gene” or worse “cause” or “cure” of say prostate cancer or melanoma. In reality one does not know whether this is a marker for cancer, a marker for a predisposition for cancer or just plain noise.

What the authors, and others, have argued is that it is essential to have a well-defined dynamic system model of how say PTEN and AKT interact and how they in turn control MYC and where the controls on p53 are in this chain. The microarray analyses should be done in the context of defining the linkages in the state model and not as ends in themselves. The model can then be validated. From such a model we can then see conditions on their way to cancer and conditions representing advanced cancers. For example, recent authors have announced a way to measure PTEN in prostate cancer and laud that as a diagnostic step. In reality by the time PTEN has been deactivated there is most likely a metastasis. Understanding and refining a model is the essence of the "why" articulated by the authors.

On p 166 there is a superb critique of what the authors call the *pre-Galilean thinkers*, namely the biologists who like Linnaeus were really just classifiers of forms and shapes failing to understand why they were what they were. One must remember that biology was all too often just a study of things and a process of naming them and classifying them. The systems which made for these differences were little understood, and worse, beyond the mindset of many who practiced in the field.

Chapter 9 is, in my opinion, the pinnacle of their argument. Simply put, we should now begin to perform our experiments within the context of a model. For example, we know many of the pathways of the key genes intracellular, but we do not yet understand the dynamic model that controls them. Thus, when we do microarray tests, we should be doing them to determine the constants in the model and then validate that design. We should, in effect, *identify* the system, using a system framework, not just some unstructured set of classifiers. We have the structures, now is the time to put them to use.

Science is iterative. It is an iterative set of models and refinements. On p 171, the authors refer to Turing's last paper on tessellation, or why zebras have stripes. The paper by Turing was submitted a day or two before he committed suicide and it was done without the benefit of Watson and Crick who were simultaneously doing their work at Cambridge. He intuited intercellular flow of some yet to be defined controlling substances. The concentration of these unknown substances would rise and fall in concentration and as such the color would change.

This approach has recently been applied, using a system model of flower genetics, and it explains and demonstrates the control of patterning in a genus of flowers. Having the model for this genus of flower, which is experimentally verifiable, one, can then do the inverse, namely the controllability issue of creating desired flower patterns. That also is the essence in cancer dynamics, namely of creating a control or cure, but with a verifiable model. One must have the model, thus say the authors. Thus says nature! If one takes the authors systems approach and applies it to intercellular systems thinking, then it can be argued that the stem cell of cancer theory as has been recently evoked can be readily explained, as readily as those zebra stripes! That is the strength of the model posited by the authors.

8. CONCLUSIONS AND OBSERVATIONS

We have introduced a new paradigm of viewing information and have developed a world view to place that construct in. The construct tries to relate the human interface problem and the structure of both information and knowledge of events into a single schema. We have addressed the issue of what is multimedia communications, what are the elements of the design process in this new medium, what is the design dictates of the total environment, and what rules for design can be abstracted from the change in the experience in interacting with media.

Whatever the ultimate design factors that may evolve, there is certain obvious design observations that can be made based upon the current understanding of the multimedia area. We must consider that in designing in a multimedia world we are doing so in a distributed service environment. It is not a manufacturing business where the product is assembled in a factory under the control of the owner and where quality can be carefully maintained and managed. It is a service assembled in the hands of a user in an environment that is neither predictable nor constant. Thus the design challenge is to incorporate the stochastic nature of the shared user environment.

To this end there are several design rules that have evolved in the process of understanding such systems. Specifically:

The next step should always be obvious.

Whenever designing a multimedia system, the presentation to the user, through whatever senses, should clearly indicate what the next step should be. Where should I type next, where can I place the pointer, which device do I use, what should I say? All too often designers let the user have the freedom to create. This results in ambiguity, frustration and visual, aural and tactile dissonance.

Form matches function.

What are we using the system for and why? What is the function and the form of the system should match the function that it has been designed for.

There should be consistent paradigms.

When the system is designed to edit images, the editing tools should be the same in all configurations. The access mechanisms, if they are on the left should always be on the left.

Execution should be smooth.

Tactile and visual dissonances are common factors in poor design. A smooth design should be such as to enhance the conversationality mode of the session.

The question should always be obvious.

State what you want. The statement should be clear and not allow for any secondary interpretation. If the question is complex, then it should be broken down into smaller segments and simpler questions. To paraphrase Wittgenstein, the essence of true understanding is the ability to pose the question in such a way that the answer is clearly "yes or no".

The answer should always be obvious.

When answering a question, the answer should always be clear and obvious. Again if a complex answer is to be presented it too should be segmented.

There should be no ambiguity of expectations.

The users and the designer should have the same set of expectations for the deployment of the system. "I never thought they would do that with it!" is a common complaint. If all else fails, listen to the customer, user, etc.

If we can develop systems that follow these guidelines in all of their dimensions, than there should be a smooth road to transition in the multimedia area.

How should we interpret these observations when we examine cancer genomics? What validity should we give to the plethora of claims of having found the gene which causes a specific type of cancer? What reliance can we have on prognostic testing of cancer genes?

As Dougherty notes:

Almost from the onset of the high-throughput microarray era, papers reporting classifiers based on gene-expression features have appeared. There have also been cautionary warnings about the dangers of misapplication of classification methods designed for use with at most hundreds of features and many thousands of sample points to data sets with thousands or tens of thousands of features (genes) and less than one hundred sample points (microarrays).

Keeping in mind the thousands of gene expressions on a microarray, consider a sampling of sample sizes for cancer classification: acute leukemia, 38 ; leukemia, 37 ; breast cancer, 38; breast cancer, 22 ; follicular lymphoma, 24; glioma, 50 (but only 21 classic tumors used for class prediction) ; and uveal melanoma, 20 . This is a tiny sampling of the host of microarray classification papers based on very small samples and selecting feature sets from among thousands of genes…..

He makes the critical point that having microarrays we can now proceed to identify one gene after another, yet we fail to have a realistic model underneath which is predictive.

We can cluster, we can apply logistic techniques to an extreme but the inherent model, the survivable paradigm, is missing.

Dougherty continues:

In this vein, the ubiquity of data mining techniques is particularly worrisome. These tend to search for patterns in existing data without regard to experimental design or predictive capability. Keller points out the danger of trying to draw grand inferences from patterns found in data. Referring to William Feller's classic text on probability theory, she writes,

"By 1971, the attempt to fit empirical phenomena to such distributions was already so widespread that Feller felt obliged to warn his readers against their overuse.... Feller's emphasis on the logistic curve as 'an explicit example of how misleading a mere goodness of fit can be' was motivated precisely by the persistence of such 'naïve reasoning'."

Data mining is often erroneously identified with pattern recognition when, in fact, they are very different subjects…

Here is the powerful statement related to Feller regarding the logistic curve. Frankly one can fit anything to anything in this model, and is it predictive? Not really. The crisis in genomics today is having too much data and getting it too easily. It is akin to having locations, times, for trillions of particles, yet having no Newtonian model to relate them to F=ma.

Thus it is essential to have models, and models which are predictive.

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