Functional Sequence Complexity (FSC)

Measured in "Fits" (Functional bits).

Scirus Sci-Topics Page

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Sequence complexity has three subsets: Random (RSC), Ordered (OSC), and Functional (FSC).[1] Functional Sequence Complexity is measured in "Fits." Fits are "functional bits."[2-4]

To understand Functional Sequence Complexity (FSC), one must first digest the essence of the other two subsets of sequence complexity. Random Sequence Complexity (RSC) lies at the opposite end of a bi-directional sequence complexity vector from Ordered Sequence Complexity (OSC).

Order		**Randomness**
OSC		RSC
←———————	**Increasing complexity**	———————→
Minimal Uncertainty		Maximum Uncertainty
Low Shannon bit content		High Shannon bit content
Maximum compressibility		Minimum compressibility
Most patterned		Least patterned

Random Sequence Complexity (RSC) is defined by an inability to compress a sequence into a representation shorter than the sequence itself. The sequence lacks any redundant order or pattern that would allow compression. With RSC, no patterns exist in the sequence either from natural law constraints or from repeated use of programming modules.

Ordered Sequence Complexity (OSC) is typically produced by law-like cause-and-effect determinism. Such forced ordering produces boring redundancy and also precludes choice contingency needed for any form of programming. Combinatorial uncertainty, freedom of selection, and

potential information instantiation are all precluded in highly ordered strings. An example of a highly ordered string is a polyadenosine that adsorbs naturally onto montmorillonite clay.[5-7] Algorithmic programming and control are made impossible when sequences are constrained by law.

Functional Sequence Complexity (FSC) is invariably associated with all forms of non-trivial formal utility. The algorithmic programming of FSC requires anticipation of the future. Purposeful choices for potential final function must be made. Mere aperiodicity of a sequence is not sufficient to define FSC. RSC is aperiodic; yet RSC produces no formal and final function.

Usually, FSC comes in the form of linear digital prescription using a symbol system. FSC requires the programming dimension of uncoerced choices for potential function at successive decision nodes in the string. RSC has mere bifurcation points, with nothing more than coin flips at each successive fork in the road to determine which fork to take. No expectation of improved trip efficiency exists when coin flips are used to determine which fork in the road to take.

Rats improve their exit time from mazes by memorizing wise purposeful choices at each successive decision node. Those choices must be made prior to the realization of any function. Utility (making it out of the maze) is only realized at the end of a long string of choices. The choices must be made IN PURSUIT OF eventual usefulness, not immediate gradification.

A succession of purposeful binary choices can be recorded as a string of symbols (e.g., 0's vs. 1's). That string of symbols represents FSC, the same as any computational program in computer science.

Thus, FSC arises only out of wise choices at true decision nodes, logic gates, and purposeful configurable switch-settings. The latter can only be set by formalism, not physicality, if sophisticated function is to be realized. In the generation of FSC, not only must each successive choice opportunity be free from physicodynamic determinism, it must be deliberately chosen en route to achieving eventual formal and final function.

Choice Determinism (CD), as opposed to Physicodynamic Determinism (PD), is quite real in producing any FSC string. The causation of FSC is formal (abstract, conceptual, and choice-based), not physical. The generation of FSC strings has never been observed to come into existence independent of agency. Zero empirical evidence exists of inanimate

physicality producing an integrated circuit, a genetic algorithm, a symbol system, language, or computational success.

No empirical evidence exists of either RSC of OSC ever having produced a single instance of sophisticated function or true organization. Algorithmic optimization requires purposeful choices to pursue eventual ideal function. Prescriptive Information (PI), circuit integration, and organization all invariably manifest FSC. Any attempt to deny the need and reality of purposeful choices precludes the production of any sophisticated function. Naturalistic philosophic presuppositions militate against acknowledging the obvious facts of reality. "Chance and Necessity" is a false dichotomy. Reality actually consists of three fundamental categories, not two: Chance, Necessity and Choice. By Choice, we do *not* mean mere Selection *FROM AMONG* [evolution]. The kind of Choice clearly observed everyday by everyone as a major component of reality includes Selection *FOR (IN PURSUIT OF)* not yet existent function.[8-11] Inanimate nature cannot exercise or generate such choice with intent. Only agency does. Mere mass/energy interactions have never been shown to produce the slightest hint of agency.

Nucleic acid genes, promoters and other regulators are examples of FSC, not OSC or RSC. The sequencing of nucleotides in single positive strands is physicodynamically indeterminate (free, unconstrained by natural law). Clearly this sequencing is not random either. Way too much sophisticated control is prescribed by all these sequences to attribute to noise. Meaningful/functional messages are also sent and received using FSC strings ("messenger molecules;" biopolymers).

From the perspective of amino-acid-sequence prescription alone, genomes are programmed using sophisticated noise-reducing block codes (Triplet codons prescribe each amino acid). The redundancy found in the codon table is misleading, however. Superimposed on triplet codon language is a second independent language involving hexamers. Intracellular languages are multi-layered, using the same symbols, but with different meanings and functions in conveyed simultaneously in each language. Coding is therefore multidimensional. The hexameric language prescribes Translational Pausing (TP).[12,13] TP in turn determines correct folding of the polyamino chain at the back door of the ribosome to produce properly folded molecular-machine proteins.[13] Both of these superimposed languages manifest FSC in the sequencing of nucleotides. Each locus in the string represents a quaternary choice from among four options.

Linear sequence complexity has received extensive study in many areas relating to Shannon's syntactic transmission theory.[14-16] This theory pertains only to communication engineering. Linear complexity was further investigated by Kolmogorov, Solomonoff, and Chaitin.[17-21] Compressibility became the measure of linear complexity in this school of thought. Hamming pursued the goal of noise-pollution reduction in Shannon's communication channel through redundancy coding.[22] Communication engineering has improved by leaps and bounds.

Little progress has been made, however, in measuring and explaining *intuitive information*. This is especially true regarding the derivation through natural process of semantic instruction. The purely syntactic approaches to sequence complexity of Shannon, Kolmogorov, and Hamming have little or no relevance to "meaning." Shannon acknowledged this in the 3rd paragraph of his first famous paper right from the beginning of his research.[15] Inadequacy is still very apparent in more recent attempts to define and measure functional complexity and information.[23-59]

Nucleic acid instructions reside in linear, digital, and resortable sequences.[60-63] Replication is sufficiently mutable for evolution, yet conserved, competent, and repairable for heritability.[64]

In life-origin science, attention usually focuses on a theorized pre-RNA World.[65-68] RNA chemistry is extremely challenging in a prebiotic context. Ribonucleotides are difficult to make and activate (charge). Oligoribonucleotides are also extremely hard to form, especially without templating. The maximum length of such single strands in solution is usually only eight to ten monomers (mers). As a result, many investigators suspect that some chemical RNA analog must have existed[69,70]. For our purposes here of discussing linear sequence complexity, let us assume adequate availability of all four ribonucleotides in a pre-RNA prebiotic molecular evolutionary environment. Any one of the four ribonucleotides could be polymerized next in solution onto a forming single-stranded polyribonucleotide. Let us also ignore in our model for the moment that the maximum achievable length of aqueous polyribonucleotides seems to be no more than eight to ten monomers (mers). Physicochemical dynamics do not determine *the particular sequencing* of these single-stranded, untemplated polymers of RNA. The selection of the initial "sense" sequence is largely free of natural law influences and constraints. *Sequencing is dynamically inert*[71].

Initial sequencing of single-stranded RNA-like analogs is crucial to most life-origin models. Particular sequencing leads not only to a theorized self- or mutually-replicative primary structure, but to catalytic capability of

that same or very closely-related sequence. One of the biggest problems for the pre-RNA World model is finding sequences that can *simultaneously* self-replicate and catalyze needed metabolic functions. For even the simplest protometabolic function to arise, large numbers of such self-replicative and metabolically contributive oligoribonucleotides would have to arise at the same place at the same time.

Little empirical evidence exists to contradict the contention that untemplated *sequencing* is dynamically inert (physically arbitrary). We are accustomed to thinking in terms of base-pairing complementarity determining sequencing. It is only in researching the pre-RNA world that the problem of single-stranded metabolically functional sequencing of ribonucleotides (or their analogs) becomes acute. And of course highly-ordered templated sequencing of RNA strands on natural surfaces such as montmorillonite clay offers no explanation for biofunctional sequencing. The question is never answered, "From what source did the *template* derive its functional information?" In fact, no empirical evidence has been presented of a naturally-occurring inorganic or organic template that contains anything more than combinatorial uncertainty. No bridge has been established between combinatorial uncertainty and utility of any kind.

Increased frequencies of certain ribonucleotides, CG for example, are seen in *post-textual* reference sequences. This is like citing an increased frequency of "qu" in post-textual English language. The only reason "q" and "u" have a higher frequency of association in English is because of arbitrarily chosen rules, not laws, of the English language. Apart from linguistic rules, all twenty-six English letters are equally available for selection at any sequential decision node. But we are attempting to model a purely pre-textual, combinatorial, chemical-dynamic *theoretical* primordial soup. No evidence exists that such a soup ever existed. But assuming that all four ribonucleotides might have been equally available in such a soup, no such "qu" type *rule*-based linkages would have occurred chemically between ribonucleotides. They are freely resortable apart from templating and complementary binding. Weighted means of each base polymerization would not have deviated far from $p = 0.25$. Dimers seem to show some physical predilections. But longer stochastic ensembles seem randomly sequenced, with no prescriptive function.

When we introduce ribonucleotide availability realities into our soup model, we would not expect hardly any cytosine to be incorporated into the early genetic code. Cytosine is extremely difficult even for highly skilled chemists to generate.[72,73] If an extreme paucity of cytosine existed in a primordial environment, uncertainty would have been greatly reduced.

Heavily weighted means of relative occurrence of the other three bases would have existed. The potential for recordation of prescriptive information would have been reduced by the resulting high probability and low uncertainty of base "selection." Self-ordering would have prevailed over complexity.

All aspects of life manifest extraordinarily high quantities of prescriptive information. Any self-ordering (law-like behavior) or weighted-mean tendencies (e.g., reduced availability of certain bases) would have limited information instantiation and retention in the sequencing.

If non-templated chemistry predisposes higher frequencies of certain bases, how did so many highly-informational genes get coded? Any programming effort would have had to fight against a highly prejudicial self-ordering physicodynamic redundancy. There would have been little or no uncertainty (bits) at each locus. Information potential would have been severely constrained.

Functional Bits (Fits)

The evolution of amino acid sequence, and its effect on biofunction, can now be quantified in "fits" (functional bits).[4]

To understand how Functional Sequence Complexity can be measured, we must first understand "Functional Uncertainty (H_f):"

> "Shannon's original formulation, when applied to biological sequences, does not express variations related to biological functionality such as metabolic utility. Shannon uncertainty, however, can be extended to measure *the joint variable* (*X, F*), where *X* represents the variability of data, and *F* functionality. This explicitly incorporates empirical knowledge of metabolic function into the measure that is usually important for evaluating sequence complexity. This measure of both the observed data and a conceptual variable of function jointly can be called *Functional Uncertainty* (H_f),[74] and is defined by the equation:
>
> $$H(X_f(t)) = - \sum P(X_f(t)) \log P(X_f(t)) \qquad (1)$$
>
> where t = a certain time and X_f denotes the conditional variable of the given sequence data (*X*) on the described biological function *f* which is an outcome of the variable (*F*)."[74]

In this approach, *f* might represent the known 3-D structure of a protein family. The entire set of aligned sequences that satisfies that protein's function, therefore, would constitute the outcomes of X_f. The advantage of using $H(X_f(t))$ is that evolutionary changes through time in the functionality of sequences can be measured.

Functional uncertainty as a measure of FSC

The measure of Functional Sequence Complexity, denoted as ζ, is defined as the change in functional uncertainty from the ground state $H(X_g(t_i))$ to the functional state $H(X_f(t_i))$, or

$$\zeta = \Delta H\,(X_g(t_i), X_f(t_j))\,. \qquad (2)$$

The resulting unit of measure is defined on the joint data and functionality variable, which we call *Fits (*or *F*unctional b*its).* The unit Fit thus defined is related to the intuitive concept of *functional* information, including genetic instruction and, thus, provides an important distinction between functional information and Shannon information.[75,76]

The limitation of Functional Sequence Complexity (FSC) measurements is that they are nonspecific averages. In addition, the change in negative Shannon Uncertainty is only obtained by the extrinsic injection of true positive information into the equation. Our probabilistic combinatorial uncertainty is educated only by the empirical data providing the relative certainty of which particular sequences will work. We sneak in through the back door, in other words, the real semantic, functional information rather than the equation generating it. The empirical data is only obtained after the fact, and in very general statistical terms.

The reason FSC does not qualify as Prescriptive Information (PI)[77] is that it cannot specifically enumerate which particular sequences will work. The latter is the real essence of intuitive, functional, prescriptive information (PI).

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