STRUCTURAL AND FUNCTIONAL DIVERSITY OF THE EUKARYOTIC GENOME

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Metaptation:
Metaphors for Genome Evolution

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Metaphor

an implicit comparison; a tool for thinking.

Metaptation

a neologism; the subject of this talk.

Image by Milo Winter
Aesop's Fables, 1919

a fable of a grasshopper . . .

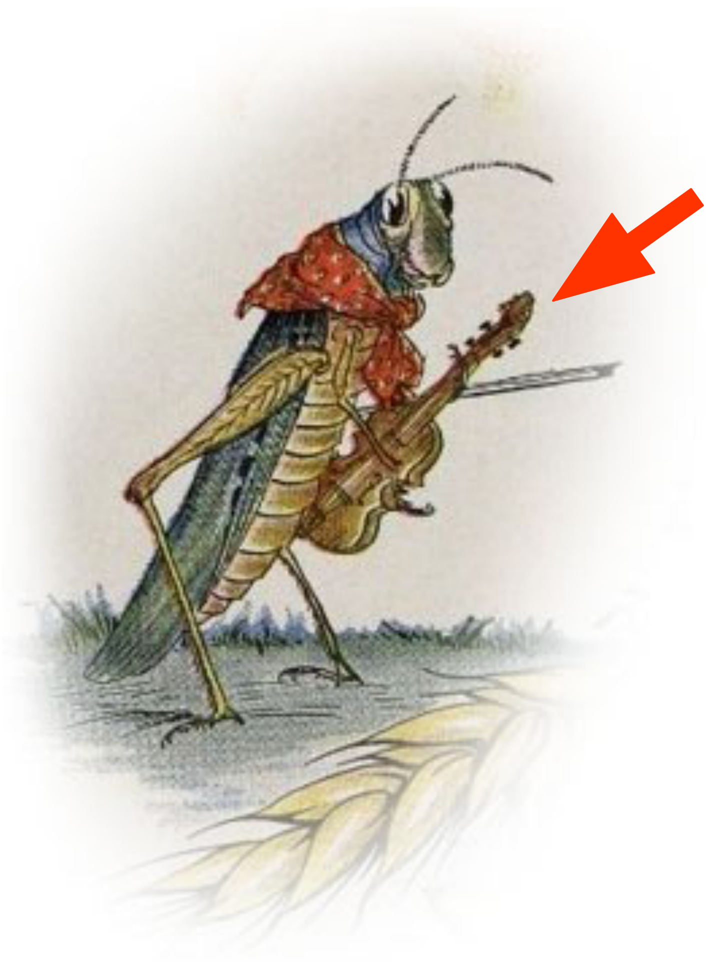

Image by Milo Winter
Aesop's Fables, 1919

Genes need
“tuning knobs” !

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Simple Sequence Repeats behave like tuning knobs.

Incremental adjustability

Repeat number mutations typically exert small effects on phenotype.

Reversibility

Any shift in repeat number can be readily reversed.

Modularity

Each example has its own characteristics.

A tuning knob has **dual functionality**.

A **concrete** function:

a “**setting**” (parameter value).

An **abstract** function:

a “**protocol**” (adjustability).

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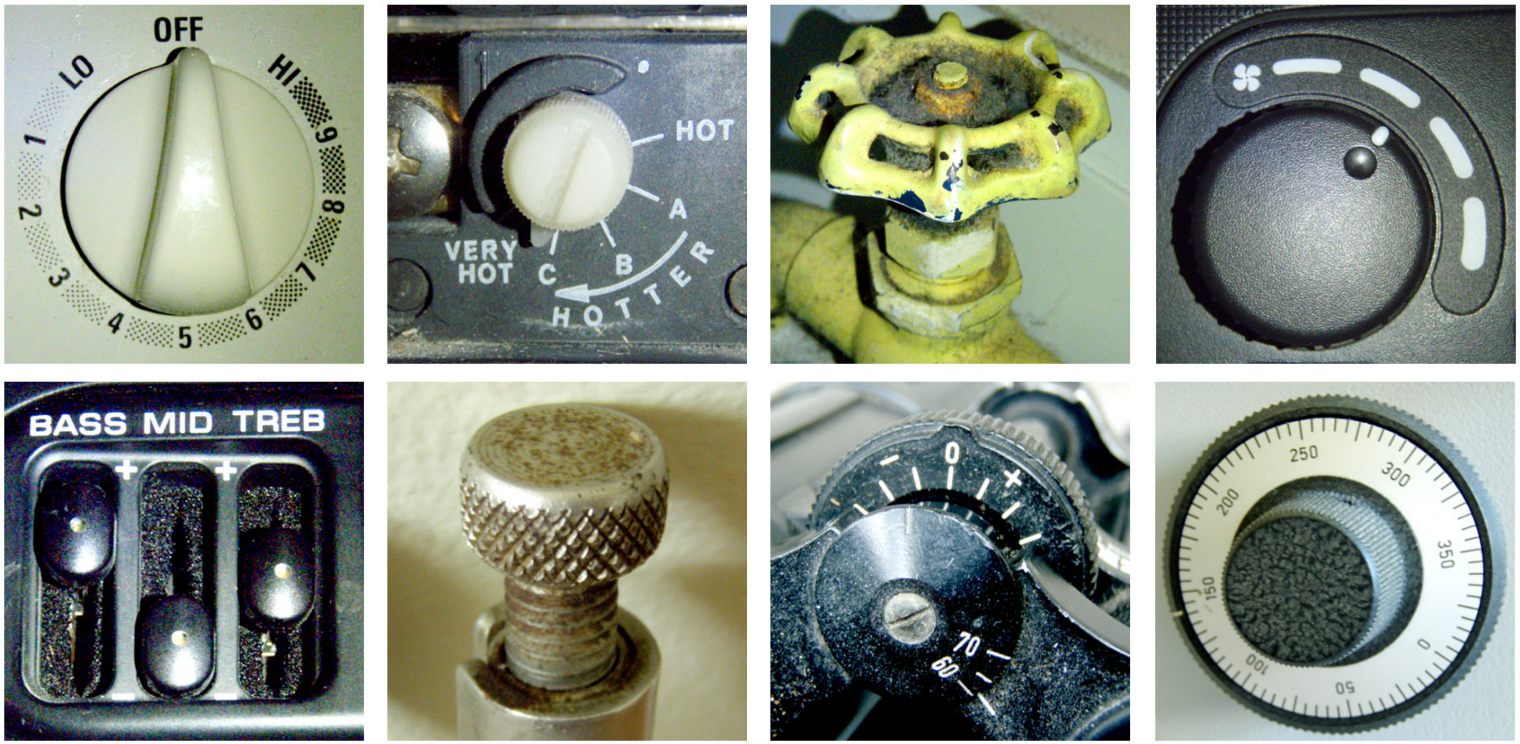
Protocol of adjustability



Protocol of adjustability
embodied by simple sequence repeats

Motifs

<u>Microsatellites</u>

mononucleotides
e.g., *polyA • polyT*

dinucleotides
e.g., AC_n • GT_n

trinucleotides
e.g., CAG_n • CTG_n

tetra-, penta-, hexanucleotides

<u>Minisatellites</u>

longer motifs, up to tens of nucleotides

Functional domains

<u>practically anywhere</u>!

exons

introns

UTRs

upstream, downstream

et cetera

A **protocol** is an implicit rule or architecture that defines permissible avenues for behavior.

A **genetic protocol** imposes "grammatical" constraints on genetic variation.

An **advantageous** genetic protocol enhances the probability of beneficial mutation.

Some advantageous protocols.

(adaptively plausible constraints on genetic variation)

Incremental adjustability (simple sequence repeats).

Cut and paste (transposable elements).

Mix and match (meiotic recombination).

Programmed gene rearrangement (e.g., trypanosomes).

On / off switching (bacterial contingency genes).

Many more . . . ?

Questions of protocol

Do evolutionary protocols ***just happen*** (by accident)?

or

Have protocols ***evolved*** because they are evolutionarily advantageous?

If protocols have evolved, how could this be possible?

A conceptual difficulty . . .

An advantageous protocol can raise the mutation rate for variation arising within the constraints of the protocol.

But the idea that mutation rates might increase for evolutionary advantage is contrary to conventional evolutionary theory.

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Natural selection of mutation rates has only one possible direction, that of reducing the frequency of mutation to zero.

Evolution has probably reduced mutation rates to far below species optima, as the result of unrelenting selection for zero mutation rate in every population.

George C. Williams

Adaptation and Natural Selection, 1966

If genetic variation arises within the constraints of a protocol, selection for those variants must **indirectly** select the protocol.

Image from Wikipedia Commons

A semantic difficulty . . .

Protocols *cannot* be adaptations, because an "adaptation" *by definition* is shaped by natural selection.

And protocols are invisible to natural selection.

Image from Wikipedia Commons

Natural selection shapes adaptations by acting on phenotypes.

Natural selection sees the grasshopper.

Natural selection cannot see the the implicit protocols in the grasshopper’s genome.

Image from Wikipedia Commons

A simple semantic solution:

If an advantageous protocol cannot properly be called an adaptation,

Let us call it a “**metaptation**.”

Image from Wikipedia Commons

An **adaptation** is an advantageous phenotypic trait.

The *process* of adaptation is how such phenotypic traits evolve, by natural selection for fitness.

* * *

A **metaptation** is an advantageous genetic protocol.

The *process* of metaptation is how protocols evolve by *indirect* selection.

Image from Wikipedia Commons

Metaptation

[*meta*, change, transcend + *aptation*, fitness]

1. an evolutionary process by which natural selection indirectly shapes genomic “protocols” that facilitate evolutionary adaptation.

2. any of the resulting “protocols for effective evolution”.

Evolutionary Theory (1985) 7:22

Image from Wikipedia Commons

A **metaptation** is a genomic pattern or architecture – a protocol – which constrains the effect of mutation and enhances the probability of adaptive benefit.

Image from Wikipedia Commons

Remaining slides below are quotations from older literature, giving historical examples of attitudes toward variation and mutation.

Image from Wikipedia Commons

What the devil determines each particular variation? What makes a tuft of feathers come on a cocks head, or moss on a moss rose?

Charles Darwin
letter to T.H. Huxley, 25 Nov 1859

A grand and almost untrodden field of inquiry will be opened, on the causes and laws of variation . . .

Charles Darwin
On the Origin of Species, 1859

In everyday usage, protocols are rules designed to manage relationships and processes smoothly and effectively.

If modules are ingredients, parts, components, subsystems, and players, then protocols describe the corresponding recipes, architectures, rules, interfaces, etiquettes, and codes of conduct.

Protocols here are rules that prescribe allowed interfaces between modules, permitting system functions that could not be achieved by isolated modules. Protocols also facilitate the addition of new protocols and organization into collections of mutually supportive protocol suites.

Thinking in terms of protocols, in addition to genes, organisms, and populations, as foci of natural selection, may be a useful abstraction for understanding the evolution of complexity.

Good protocols allow new functions to be built from existing components and allow new components to be added or to evolve from existing ones, powerfully enhancing both engineering and evolutionary "tinkering." Successful protocols become highly conserved because they both facilitate evolution and are difficult to change.

Marie Csete and **John Doyle** 2002 (*Science* 295:1664)

Far from being clumsy stumblers into random point mutations, genomes have evolved mechanisms that facilitate their own evolution.

These mechanisms diversify a genome and increase the probability that its descendants will survive.

Lynn Helena Caporale 1998 (*Annals N.Y. Acad. Sci*. 870)

Any organism as it now exists must be regarded as a very complex physicochemical machine with delicate adjustments of part to part. Any haphazard change made in this mechanism would almost certainly result in a decrease of efficiency.

Only an extremely small proportion of mutations may be expected to improve a part or the interrelation of parts in such a way that the fitness of the whole organism for its available environments is increased.

Bridges 1919 (*J Exp Zool* 28 [3]: 37)

It seems at first glance that there should be a counter-selection, due to the occurrence of favorable mutations. It is true that favorable mutations furnish the only basis for improvement of the race, and must be credited with being the only raw material for evolution. It would evidently be fatal for a species, in the long run, if its mutation rate fell to zero, for adjustment to changing conditions would then not long remain possible. While this effect may occur, it is difficult to imagine its operation. . .

[F]or every favorable mutation, the preservation of which will tend to increase the number of genes in the population that raises the mutation rate, there are hundreds of unfavorable mutations that will tend to lower it. Further, the unfavorable mutations are mostly highly unfavorable, and will be more effective in influencing the rate than will the relatively slight improvements that can be attributed to the rare favorable mutations.

[W]hy does the mutation rate not become reduced to zero? No answer seems possible at present, other than the surmise that the nature of genes does not permit such a reduction. **In short, mutations are accidents, and accidents will happen**.

Sturtevant 1937 (*Q Rev Biol* 12: 464)

One frequently hears that natural selection will not produce too low a mutation rate because that would reduce the evolutionary plasticity of the species.

[N]atural selection of mutation rates has only one possible direction, that of reducing the frequency of mutation to zero. That mutations should continue to occur requires no special explanation. It is merely a reflection of the unquestionable principle that natural selection can often produce mechanisms of extreme precision, but never of perfection. . .

Evolution has probably reduced mutation rates to far below species optima, as the result of unrelenting selection for zero mutation rate in every population.

George Williams
Adaptation and Natural Selection, 1966

[I]t can be appealing to suppose that the genomic mutation rate is adjusted to a level that best promotes adaptation. Most mutations with phenotypic effects are harmful, however, and thus there is relentless selection within populations for lower genomic mutation rates. Selection on beneficial mutations can counter this effect by favoring alleles that raise the mutation rate, but the effect of beneficial mutations on the genomic mutation rate is extremely sensitive to recombination and is unlikely to be important in sexual populations.

The physiological cost of reducing mutation below the low level observed in most populations may be the most important factor in setting the genomic mutation rate in sexual and asexual systems, regardless of the benefits of mutation in producing new adaptive variation. Maintenance of mutation rates higher than the minimum set by this 'cost of fidelity' is likely only under special circumstances.

Sniegowski et al. 2000 (BioEssays 22:1057)

Some authors believe it to be as much the function of the reproductive system to produce individual differences, or very slight deviations of structure, as to make the child like its parents.

Charles Darwin
On the Origin of Species, 1859