Evolution in Four Dimensions

Chapters 1-3

Outline by John Protevi of
Eva Jablonka and Marion Lamb, *Evolution in Four Dimensions: Genetic, Epigenetic, Behavioral, and Symbolic Variation in the History of Life* (MIT, 2005)
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Chapter 1: The Transformations of Darwinism

JL = Jablonka and Lamb
Evolution = change in historical series of entities
NS = natural selection (mechanism of evolution)
ENS = evolution by natural selection
IAC = inheritance of acquired characteristics
EIHV = environmental induction of heritable variation
CM = chromosomal material

I) Intro: controversies in science and in biology
  A) Darwin had little to say about nature and causes of hereditary variation
  B) JL will trace history of gene-centered versions of Darwinism
II) Darwin's Darwinism
  A) Laws of Evolution by Natural Selection (ENS)
    1) Darwin's version of ENS
      a) Reproduction
      b) Inheritance
      c) Variability
      d) Struggle for Existence
    2) Maynard Smith's generalization of ENS
      a) Multiplication
      b) Variation
      c) Heredity
      d) Competition
    3) With Maynard Smith's generalization
      a) No need to know anything about
        i) Processes of heredity and multiplication
        ii) Origins of heritable variation
        iii) The nature of the entity that evolves through NS
      b) Thus it can in theory be applied to many systems (warning: many debates here!)
        i) Cosmology
        ii) Economics
        iii) Culture
  B) Darwin and heritable variation via "effects of life on organism and 'use and disuse'"
    1) Sounds like Lamarck
      a) Inheritance of acquired characteristics (IAC)

b) Shown to be wrong by Darwin's theory of NS
2) But the usual story about Lamarck is wrong
a) What's wrong about it?
i) Lamarck was not a simpleton
ii) Lamarck did not invent idea about IAC
iii) Darwin had a role for "use and disuse" in his theory
iv) Darwin's theory of NS did not displace IAC
b) What's the real story?
i) Lamarck was a sophisticated thinker and didn't solely focus on IAC
ii) Almost all biologists believed in IAC throughout 19th C
iii) Darwin believed in IAC
iv) NS was not the reason IAC was displaced

C) Darwin's theory of heredity: pangenesis
1) Gemmules as units of heredity and development
a) Tiny particles spread throughout body
b) In sexual beings, gemmules accumulate in reproductive organs
i) Gemmules join in sperm and egg before development
ii) Offspring are a blend of parental characters
iii) What is inherited is the actual character
iv) Some gemmules are dormant and awake in later generations
v) "inheritance = form of growth"
2) But what accounts for variation, since with blending, you should get uniformity?
a) The theory: environmental change can "induce" variation
i) Change in nutrition / climate affects growth
(a) Alters proportion of gemmules in reproductive organs
(b) Awakens dormant gemmules
ii) Changed conditions change gemmules themselves
b) The result: Darwin's theory allows for IAC

D) Conclusion by JL: EIHV does NOT weaken evolution by NS
1) In fact, EIHV increases
a) Amount of variation
b) Scope of NS
2) Generality of theory of evolution by NS is not limited to
a) Any one theory of mechanism of heredity
b) Any one theory of causes of variation

III) Weismann's Neo-Darwinian Theory: Acquired Characteristics Discarded
A) Three great advances in mid-19th C biology
1) Cell theory (Virchow)
2) Evolution by NS (Darwin)
3) Refutation of spontaneous generation (Pasteur)

B) Linking cell theory to heredity / development / evolution (Weismann)
1) Once chromosomal material was identified as hereditary / developmental substance
2) Then mitosis must be distinguished from meiosis
a) Mitosis: division of ordinary [eukaryotic] cells:
i) Doubling then division of chromosomes
ii) Splitting of cell into two daughter cells
iii) Each daughter cell
(a) Inherits one half of the doubled material
(b) That is, a full batch of chromosomal material (CM)
iv) But that creates problems for reproduction
(a) If sperm and egg are produced by mitosis

(b) Then each have full complement of CM
(c) And the fertilized egg would have double amount of CM!

b) Meiosis: "reduction division" in production of sperm and egg
i) Each daughter cell (sperm or egg) receives only half CM
ii) So the fertilized egg will have the normal full complement of CM

C) Weismann rejects IAC
1) No way for properties of somatic cells to be transmitted to sperm or egg cells
2) Thus we have the continuity of the germ plasm
a) Segregation of germ plasm early in development for separate production of sperm / egg
b) Partial inheritance of "determinants" as answer to cell differentiation
i) Each embryonic cell receives a different part of nuclear material
ii) So the nuclear material should be getting simpler as cell differentiation proceeds
iii) Only the germ plasm in germ line retains full complement of determinants

D) Source of variation for Weismann
1) Sexual reproduction involves mingling germ plasm from parents
a) Which means there's a long history of mingling from ancestors
b) Now half of CM eliminated in meiosis is not same for every sperm / egg
c) Thus we have rich source of variability from mingling and meiotic "reshuffling"
2) But what was original source of variation?
a) Random accidents alter determinants
b) Leading to "germinal selection" via changes in nutrition / temperature etc.
i) Environment has heritable effects via direct action on germ plasm
ii) Unit of selection issue:
(a) Not just individual organism
(b) But determinants in germ plasm
(c) Cells w/in a tissue
(d) Groups

E) Summary: differences btw Weismann and Darwin
1) Weismann gives NS an exclusive role, rejecting IAC
2) Weismann had different hereditary theory (determinants vs gemmules)
3) Weismann source of hereditable variation via effects on determinants in germ line
4) Weismann focused on sexual reproduction as producing heritable variation

IV) Doubts about Darwinism
A) Neo-Lamarckians:
1) Progressive / goal-directed evolution
2) Herbert Spencer: evolution in many developmental processes / belief in IAC
3) Lacked a good theory of heredity

B) Gradualism vs discontinuous evolution
1) Can Darwin's notion of gradual evolution through selection of small variation account for continuously varying traits or must we think in terms of saltatory "sports"?
2) What about speciation? There doesn't seem to be continuity here, but gaps!
a) De Vries proposes "mutation" as accounting for sudden, discontinuous speciation
b) So many evolutionary biologists at this time didn't bother with either Lamarck or Darwin

V) The Modern Synthesis: Development Vanishes
A) Synthesis of Weismann's ultra-Darwinism and Mendlian genetics
B) Theory of heredity in the Modern Synthesis
1) Gene as "hereditary unit of biological information" determining development
2) Alleles: different versions of each gene (inherited from each parent)
3) Mendel's laws
a) Two alleles separate in formation of gametes in same condition as entering parent body
b) Alleles belonging to different pairs segregate independently

4) Dominants and recessives: hybrids do not show intermediates
5) Genes were located on the chromosomes, likes beads on a string

C) Mendelian genetics based on analysis of (visible) differences
1) At first, genetics seemed to reinforce non-Darwinian discontinuous evolution
2) But later it was shown genes can account for continuous variation
a) When characters are controlled by many genes
b) Each having a small effect

D) Mendelian genetics has no explanation for development
1) Genes located only in nucleus: ignored role of cytoplasm
2) Morgan and *Drosophilia*
3) Johansen
a) Phenotype / genotype distinction
i) All individuals in a pure line have same genotype
ii) Phenotype depends on interaction of genotype and environment
b) Genes
i) Pass on "potential for characters"
ii) Unit of information about potential phenotype
iii) Unaffected by use of that information in development
iv) Very stable, though open to occasional mutation

E) ENS according to the Modern Synthesis
1) Heredity =
a) Transmission of germ-line genes
b) Located on chromosomes (nuclear focus)
c) Discrete unit of information about character
2) Variation =
a) Consequence of random combinations of alleles through sexual reproduction
b) Each allele has small effect on characters
c) Mutations in genes are result of accidents
d) Genes are not affected by their use in development
3) Selection
a) Occurs at phenotype level
b) Alleles accumulate in population through phenotypic selection

F) Complaints by embryologists and plant biologists
1) Nuclear genetic material is not the only important thing
2) Cytoplasm is important for both heredity and development

VI) Molecular Neo-Darwinism: The Supremacy of DNA
A) Triumph:
1) DNA steps to the fore as mechanism of heredity and development
a) Hereditary gene = nucleotide string
b) Developmental gene = protein synthesis (via mRNA)
2) "Central dogma" = unidirectional information flow

B) Needed nuances
1) Non-nuclear inheritance in cytoplasmic organelles (mitochondria / chloroplasts)
2) Breakdown of one-to-one allele / protein relation
a) Many allelic variations can produce same protein
b) And many differences in amino acid strings in proteins persist in population
c) Thus many differences in proteins and alleles are "selectively equivalent"
3) "Junk DNA" or non-coding DNA
a) Some non-coding DNA is regulatory (controls gene expression) but not all!
b) Hereditary information becomes genetic program, not just genes as discrete units

C) ENS according to the Molecular Revolution

1) Gene = unit of heredity = DNA string
2) Inheritance = DNA replication
3) Cytoplasmic organelles have own DNA
4) Mutations = changes in DNA sequence via
    a) Mistakes in DNA replication
    b) Chemical / physical damage to DNA w/ improper repait
    c) Movement of DNA itself
    d) Mutagens do not increase adaptive variations
    e) So induced variation is blind / random

VII) Selfish Genes and Selfish Replicators: unit of selection controversy

A) Altruism
    1) Explanation through group selection
    2) Attack on group selection by mathematical arguments
        a) At first successful
        b) But then others claim math proof of possibility of group selection
    3) Kin selection: Hamilton
B) Dawkins and the "gene's eye view" or "selfish gene"
    1) Genes are units of inheritance *and* selection (bcs of stability and permanence)
    2) Replicators vs vehicles
    3) Replicators can unify biology, bcs they are units of
        a) Heredity
        b) Variation
        c) Selection
        d) Evolution
        e) Development
    4) They can even unify biology and sociology / psychology if we accept "memes"
C) Attacks on Dawkins
    1) Defenders of other targets of selection (individuals / kin / groups) still are gene-centered
    2) In that they agree that hereditary genes are in control of development
    3) Gould: gene-centered evolution is just "bookkeeping"
        a) Individuals / groups / species are targets of selection (bcs they survive / reproduce)
        b) NS is not the only agent of evolution
            i) Historical events (climate changes)
            ii) Accidents affecting genetic variation
            iii) Evolution is constrained by development (if organism isn't viable, it can't reproduce)
            iv) Side effects or "spandels" are possible (adaptationist debate)
    4) Gould and Dawkins agree
        a) Gene-centered heredity relevant to non-human organisms
        b) No such thing as IAC

VIII) The Transformations of Darwinism

IX) Dialogue

A) A-Life discussion: "limited heredity systems"
B) Dawkins
    1) Unit of heredity / selection:
        a) Dawkins: replicators must have high replication fidelity, which individuals don't have
        b) Response: no one said individual was unit of heredity and selection: it's the trait
    2) Relation of inheritance and development
        a) Dawkins: assumes unidirectional influence from replicators to vehicles, but not inverse
        b) Response: development does impinge on heredity
    3) Unit of heredity
        a) Dawkins: the gene is only biological hereditary unit

b) Response: there is epigenetic inheritance

C) Molecular revolution
1) It's progress to be able to speak at the molecular level
2) But there are physiological and behavioral levels of heredity as well (not just cytoplasmic)

D) Ideology
1) Surely the Modern Synthesis isn't ideological like Lysenko?
2) Of course, but "ideology" can be "assumptions" from "socio-political general worldview"

Chapter 2: From Genes to Characters

I) Intro
A) Relation of genes and development is very important today
B) JL forecast:
1) Epigenetic inheritance is important too
2) Question of information in different inheritance systems:
a) What kind of info is transmitted
b) Mechanism of info transmittal
c) Extent and fidelity of info transmittal
d) Effects of transmitted info

II) From DNA to Proteins
A) Heredity: DNA replication is a property of the cellular system, not of DNA alone
B) Function: DNA codes for proteins
1) Transcription = splitting of double helix and production of primary RNA transcript
2) Splicing = introns and exons
3) Transport = exit from nucleus and entry into cytoplasm
4) Ribosome = site of protein production
5) Translation = formation of a polypeptide chain (amino acids)
C) Noncoding DNA
1) Regulation of gene activity
2) But the cell is involved in this regulation process, which means environment contributes too

III) Digression: What is Information?
A) Two types of DNA info
1) Coding for proteins
2) Attachment sites for regulatory molecules
B) JL definition of information:
1) Correlation of changes in receiver's functional state with form and organization of source
2) This is "interpretation"
3) Source remains unchanged by such interpretation by receiver
C) DNA information
1) Characteristics:
a) Linear and modular
b) Replication is insensitive to content (vs. learning)
2) Consequences:
a) A lot of raw material for NS can be generated
b) But "nonsensical" DNA can also be generated and transmitted

IV) Genes, Characters, and Genetic Astrology
A) Monogenic diseases (one-to-one gene / trait determinism)
1) Are quite rare
2) But are a popular model for *all* gene action in development (= "genetic astrology")
B) Correlation is not causation in complex systems

V) The Tangled Web of Interactions

A) Example of APOE gene and coronary artery disease
B) Conclusions
    1) Cannot just add average effects of genes in a population and predict individual profiles
    2) Defeat of genetic determinism
        a) Developmental plasticity = many phenotypes from "same" genotype
        b) Canalization = same phenotype from "different" genotype
C) Waddington and the epigenetic landscape
    1) Developmental canalization
    2) Multiple genetic effects
D) Knockout gene experiments often produce no phenotypic differences
    1) Reasons:
        a) Duplicate genes
        b) Functional replacements
        c) Dynamic regulatory networks can adapt
    2) Results
        a) Demonstrates structural and functional redundancy in genome
        b) Developmental canalization
        c) Selectively neutral alleles
        d) It's the "evolved network of interactions" that accounts for canalization
            i) NB: genetic regulatory network (includes epigenetic factors) is unit of evolution
            ii) Not the hereditary gene as DNA sequence

VI) Genes in Pieces
A) Splicing:
    1) Excision of introns and splicing of exons
    2) The limits of introns and exons are not fixed
    3) The decisions are made by the network
        a) Developmental (cytoplasmic & intrasomatic) & environmental (extrasomatic) conditions
        b) Regulatory genes
B) Results: can no longer identify hereditary gene as locus of developmental control

VII) Changing DNA in Development
A) This is "natural genetic engineering"
B) Discussion of Weismann and chromatin diminution
C) This discussion has been only about development of somatic cells
    1) Though it's fascinating that development can change DNA ("recipe")
    2) What about evolution?
        a) Are there developmentally induced heritable changes to DNA in the germ line?
        b) IOW, are there directed changes in variation for NS? This would be Lamarck's revenge!

VIII) Dialogue
A) Language and DNA have same structure
    1) Modular
    2) Content-indifferent replication
    3) Encoded information
    4) Allows unlimited heritable variation
B) Population averages mask individual variation, but organisms live as individuals!
C) Problems with prediction:
    1) Hyper-astronomical number of permutations
        a) Genetic interaction
        b) Gene – environment interaction
    2) Cannot define "environment"
    3) Social environments are "partially constructed by individuals"
D) Must shift focus to dynamic / flexible / fuzzy networks

E) Focus on DNA alone is politically loaded
F) DNA focus allows fight against monogenic diseases
G) Effects on our thinking about evolution from focus on relation of genes / development
    1) Channels and limits our thought about evolutionary mechanisms so that we focus on "selection for the developmental, physiological, and behavioral stability and flexibility of genetic and cellular networks."
        a) Controversy over genetic determinism / selectionism
            i) Genetic determinism = thesis about development
            ii) Genetic selectionism = thesis about evolution
        b) Plasticity and canalization = network properties, not gene properties
    2) DNA can change in response to environmental cues
        a) Systems of nonrandom DNA change
        b) Formation of heritable DNA variation
        c) Transmission of such variation

Chapter 3: Genetic Variation: Blind, Directed, Interpretive?

I) Intro: John Cairns reintroduces question of directed (i.e., non-random) mutation
    A) In retrospect, Cairns was wrong with his example, but opened door to research on mutation
    B) JL will now claim that not all mutation is random, as previously believed
        1) Variation through sex
        2) Variation through mutation
        3) [NB: Lynn Margulis proposes symbiogenesis as major source of variation for evolution; mutations only modulate these major changes.]
II) Genetic variation through sex and sexual reproduction
    A) Sources
        1) Mixing genes from 2 nonidentical parents
        2) Meiosis: assignment of which chromosomes to gamete is random and independent
        3) Recombination of genes during "cross-over"
    B) What is the evolutionary advantage of sexual reproduction?
        1) Prevent accumulation of bad mutations
        2) Faster evolution in changing and selective / competitive environments
    C) Spectrum of modes of sexual and asexual reproduction: subject to evolution via NS
    D) Sex as genetic exchange is not always tied to reproduction (e.g., bacteria)
III) Variation through mutation
    A) Tradeoff between reliability and flexibility of DNA
    B) NS for "DNA-caretaker genes" for proof-reading and editing / correcting of DNA replication
IV) Randomness questioned
    A) Traditionally assumed that mutations are non-adaptive "mistakes," most of which are harmful
    B) Now, we have question of "directed mutation"
        1) We have seen developmental changes in DNA
        2) McClintock proposed genome as "organ of cell" that "responds … by restructuring genome"
        3) This is "stress-induced mutagenesis": affecting the maintaining / repairing system for DNA
    C) Thought experiment: three types of response to change
        1) Conservative:
            a) Heuristic strategy: Always and only try the traditional response
            b) Biological method: use physiological response and wait for lucky mutation at natural rate
            c) Prospects for success: works in slight changes, but in radical changes not very helpful
        2) Exploratory:
            a) Heuristic strategy: try whatever is imaginable
            b) Biological method: increase rate of random mutation

        c) Prospects for success: depends on population size
    3) Interpretive:
        a) Heuristic strategy: stick to tradition when you can; cautiously interpret when you must
        b) Biological method: non-random, but not-precisely-directed mutation
        c) Prospects for success: seems to be good, as this strategy is selected for in many cases [?]

V) Acquired, Required, Interpretive Mutations
- A) Four types of non-random mutation
    1) Induced global mutation
    2) Local hypermutation
    3) Induced local mutation
    4) Induced regional increased mutation
- B) These fit into a spectrum between "blind" and "developmentally regulated" genetic change

VI) Evolved genetic guesses
- A) Can no longer clearly distinguish instruction (development) and selection (evolution)
    1) E.g., immune system changes are developmental and selective (Edelman)
    2) Some evolutionary change (e.g., bacterial) are instructive
    3) So Lamarck is back in the picture
- B) Development, heredity, and evolution are intertwined

VII) Dialogue
- A) Stress-induced increase in recombination in specific regions of chromosomes
- B) Central dogma outlawing of backtranslation (changes from proteins to DNA)
    1) Backtranslation is not necessary for many types of IAC, which do not involve amino acids
    2) Most cell responses to changed conditions target regulatory and not coding sequences
    3) Most altered proteins due to changes in splicing / translation, not in coding sequences
- C) So, most genetic change affecting gene expression
    1) Alter number of copies of genes
    2) Control sequences
    3) Gene location on chromosome
- D) Why not more directed mutation? Because educated guesses are better than pure instruction.
- E) How are induced adaptive changes possible, as they require phenotypic feedback?
    1) In bacteria, this is easy to imagine
    2) In complex multicellulars, it's very unlikely to have mechanisms for directed genetic change
        a) Bcs. of complex interactions, such genetic change = "random" phenotypic effect
        b) But not all inheritance is genetic!
        c) So we can have IAC in other inheritance systems
            i) Epigenetic
            ii) Behavioral
            iii) Symbolic