A Paradigm Shift in Genetics: 
From Classical to New Genetics Based on Semiotics and Wave-Particle Complementarity

Sungchul Ji, Ph.D.
Department of Pharmacology and Toxicology
Ernest Mario School of Pharmacy
Rutgers University
Piscataway, N.J. 08854
sji@rci.rutgers.edu
Most biologists believe that the wave-particle duality discovered in the early decades of the 20th century applies only to fundamental particles in physics but has little to do with biology, including genetics.

This presumption has long justified biologists’ preoccupation with the study of the particle aspect (i.e., equilibrium structures) aspect of living processes, ignoring the role of waves (or dissipative structures) in life.

But two recent developments strongly indicate that the principle of wave-particle duality (or complementarity) applies to living processes, including enzymology, cell biology and genetic inheritance:

1) *The mathematical derivation of the genetic code from 4 nucleotides based on the same mathematical tools (i.e., matrix algebra) used to study oscillations, waves, and resonances* [16].

2) *The derivation in 2008 at Rutgers of the so-called PDE (Planckian Distribution Equation) that has been found to fit long tailed histograms generated in the fields of protein folding, single-molecule enzymology, cell metabolism and brain neuroscience* [2], PDE having two terms one representing the number of standing waves and the other the average energy of the standing waves.

Semiotics developed by the American chemist, logician and philosopher Charles S. Peirce (1839-1914) (see Slide #3) is the science of signs which is thought to be applicable to genetics by an increasing number of biologists since DNA is a molecular sign.

According to Brian Josephson, a Nobel Laureate in physics in 1973 (see Slide # 5), semiotics will eventually overtake quantum mechanics just as quantum mechanics overtook classical mechanics (see the Josephson conjecture in [2, Chapter 4]).

The main objective of this presentation is to marshal the evidence to support the suggested paradigm shift from the particle/structure-centered genetics of the past decades to a new genetics that is based on both particle and waves.
“... The undertaking which this volume inaugurates is to make a philosophy like that of Aristotle, that is to say, to outline a theory so comprehensive that, for a long time to come, the entire work of human reason, in philosophy of every school and kind, in mathematics, in psychology, in physical science, in history, in sociology, and in whatever other department there may be, shall appear as the filling up of its details. The first step toward this is to find simple concepts applicable to every subject.” [1]

PSC’s underlying New Genetics:

1. Irreducible Triadic Relation (ITR), the principle of semiotics (Peirce, ~1910) [2, Chapter 9].
2. Dissipative vs. equilibrium structures (Prigogine, ~1960) [3, Chapter 3]
3. Gnergy as the complementary union of information (gn-) and energy (-ergy) (Ji, 1991) [4, pp. 152-156]
4. The wave-particle complementarity (Bohr, ~1930) [5, pp. 33-40; 6]
5. The Fourier theorem (Fourier, 1807) [7]
6. PDE (Planckian Distribution Equation) (Ji, 2008-2012) [3, Section 12.12; 8]
#4  Peirce’s Simple Concepts (PSC) Underlying New Genetics

<table>
<thead>
<tr>
<th>Pioneers</th>
<th>J. Fourier</th>
<th>C. S. Peirce</th>
<th>N. Bohr</th>
<th>I. Prigogine</th>
</tr>
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</table>

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<tr>
<th>PSC</th>
<th>Fourier theorem (Complex waves can be formed from sine waves)</th>
<th>ITR (Irreducible Triadic Relation)</th>
<th>Complementarity (Wave-particle complementarity)</th>
<th>Dissipative Structures (or Dissipatons) [3, p. 76]</th>
</tr>
</thead>
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<tr>
<th>Fields</th>
<th>Mathematics</th>
<th>Semiotics</th>
<th>Physics</th>
<th>Chemistry</th>
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</thead>
</table>

*Neo-Semiotics* [2, Section 6.6.4]  
*Category Theory of Everything* (cTOE) [3, Chapter 21]
The Josephson Conjecture [2, Chapter 4]

#5

British Physicist, Cambridge University

Nobel Prize in Physics, 1973

(1940- )

“Semiotics will eventually overtake quantum mechanics in the same way as quantum mechanics overtook classical physics.” [9]

Since biology is a domain of quantum mechanics, semiotics will also overtake biology. – S. Ji

"A sign, . . . , is something which stands to somebody for something in some respect or capacity."

“I now limit it, so as to define a sign as anything which is on the one hand so determined (or specialized) by an object (see Step f) and on the other hand so determines (Step g) the mind of an interpreter of it that the latter is thereby determined mediately (Step h), or indirectly, by that real object that determines the sign . . . . The determination of the Interpreter's mind I term the Interpretant of the sign . . . “

http://www.iupui.edu/~arisbe/rsources/76DEFS/76defs.HTM

\[
\begin{array}{cccc}
  f & \quad g & \quad \text{Interpretant} \\
  \text{Object} & \quad \text{Sign} & \quad ^{\wedge} \\
  & \quad \text{Sign production} \\
  & \quad \text{Sign interpretation} \\
  & \quad \text{information flow or correspondence}
\end{array}
\]
Figure 4.5. A diagrammatic representation of the triadic definition of the sign according to C. S. Peirce (1839-1914). \textbf{Sign} = Anything that stands for something other than itself. Also called \textit{Sign Vehicles} or \textit{Representamen}. \textbf{Object} = Something referred to by a Sign. \textbf{Interpretant} = The effect that a sign has on the mind of the interpreter or sign processor. \( f = \) Sign production; \( g = \) Sign interpretation; \( h = \) correspondence or information flow.

Figure 1. DNA as a molecular sign in the sense of Peircean semiotics [2, Chapter 6]. (Top) A triangular representation of the irreducibly triadic relation (ITR) among DNA, phenotype, and cell state. (Bottom) A 3-node network representation of the ITR. $f =$ encoding; $g =$ gene expression; $h =$ evolutionary selection. The three mappings, $f$, $g$ and $h$ are thought to satisfy the commutative condition that “$f$ followed by $g$ leads to the same results as $h$”, denoted as $f \times g = h$. Thus defined, the 3-node network is equivalent to the commutative triangle of category theory in mathematics.
#9 DNA as the Rosetta Stone of the 21\textsuperscript{st} Century

<table>
<thead>
<tr>
<th></th>
<th>Human Genome</th>
<th>Rosetta Stone</th>
</tr>
</thead>
<tbody>
<tr>
<td>\textit{Produced}</td>
<td>2~3 million years ago</td>
<td>2,000 years ago</td>
</tr>
<tr>
<td>\textit{Discovered in}</td>
<td>20\textsuperscript{th} century</td>
<td>1799</td>
</tr>
<tr>
<td>\textit{Unknown sign}</td>
<td>DNA text written in deoxyribonucleotides in the nucleus of the cell</td>
<td>Egyptian hieroglyphic text written in pictographs on the surface of the Rosetta Stone</td>
</tr>
<tr>
<td>\textit{Known sign}</td>
<td>Human Genome Map</td>
<td>Demotic and Greek texts</td>
</tr>
<tr>
<td>\textit{Copernican Revolution}</td>
<td>The cell language theory [2, 10] suggesting that the DNA texts are both “phonograms”, i.e., conformational strains carrying energy, and “ideograms”, i.e., nucleotide sequences carrying information.</td>
<td>The \textit{cartouche} containing the name of Pharaoh Ramsey written in Coptic indicating that Egyptian hieroglyphs are not only ideograms but also phonograms.</td>
</tr>
</tbody>
</table>
Figure 4.6. A suggested isomorphism between the decoding of the Rosetta Stone and the decoding of the cell language. “Micro-macro coupling” indicates the postulate that the molecular properties of the cell are coupled to (or mutually dependent on) the macroscopic, behavioral properties of the human brain.

(Reproduced from S. Ji, Cell Language Theory, World Scientific, 2017)
DNA as a Carrier of Genrgy

• Before Champollion solved the mystery of the Egyptian hieroglyphs in 1822, Egyptologists believed that the hieroglyphs were *logograms*, but Champollion discovered that the Egyptian hieroglyphs were both *logograms* (representing symbolic *information*) and *phonograms* (representing physical *energy*), i.e., 'logophonograms' (see Table 4.8, Slide #14).

• Analogously, most contemporary biologists now think that DNA carries *information only* and no *energy*. However, there is now abundant evidence (reviewed in my book, *The Cell Language Theory*, World Scientific, in press), both experimental (e.g., DNA *supercoils*; see upper left corner of Slide 12) and theoretical (e.g., genes as *molecular machines*), indicating that DNA carries both *information* and *energy*, i.e, *conformons* (see Tables 4.9 and 4.10, Slides #14 and #15).

• Since *DNA* and *genes* are more or less synonymous, we can now say that genes carry not only *heritable information* (as widely believed) but also *mechanical energy* to express the information, as proposed by the "gene-as-molecular-machine" hypothesis (Ji, 1991, 2012), which is equivalent to saying that "genes carry conformons".

• Thus, it is possible that the theoretical work that I have done during the past 4 decades provides a strong support for a paradigm shift in genetics, which may be characterized as the following shift.

  **From DNA as the carrier of information to DNA as the carrier of information-energy, or gnergy.**
Three Languages on the Rosetta Stone – one Unknown and two Known – all referring to the same object, i.e., the Decree of Memphis
Figure 4.7. (a) The Rosetta stone carrying known texts (written in Demotic and Greek) and an unknown text (written in Egyptian hieroglyphs), all referring to the same Decree of Memphis. (b) The human brain contains an unknown language (DNA-based cell language or cellse) and a known one (human language or humanese), both sharing the same set of semiotic principles. Just as Rosetta stone contained two scripts, one known and the other unknown, so it is postulated that the human brain contains a known script (written in humanese) and unknown script written in cellse. It is further postulated that these two kinds of scripts share a common set of physical laws and evolutionary rules, thereby exhibiting an isomorphism [19-23]. It is because of this isomorphism between the two kinds of languages that we can hope to infer the semantics of the cell-language texts (see the left-hand box in (b)) by comparing them with associated human linguistic texts (see the right-hand box in (b)). The key elements of this comparison are summarized in Table 4.10.
Table 4.8. Three classes of written signs in Egyptian hieroglyphs, extracted from [258] and [259]. The term “logophonogram” used here is coined to indicate a symbolic sign (-gram) with the dual function of carrying meanings (logo-) as well as acting as a phoneme (-phono-). It is suggested here that the molecular analogs of logophonograms are conformons. (Reproduced from S. Ji, Cell Language Theory, World Scientific, 2017)

<table>
<thead>
<tr>
<th>Logograms (A)</th>
<th>Phonograms (B)</th>
<th>‘Logophonograms’ (C)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Iconic signs for a woman and a boy placed as the end of a hieroglyphic name to indicate the sex of the person named.</td>
<td>All the hieroglyphic signs in the name of Cleopatra, Ptolemy, and Alexander.</td>
<td>The circle-and-a-dot symbol appearing in the name of the Pharaoh Ramses stands for i) the sun called ‘rah’ in Coptic, and ii) the phoneme ‘r’ in Egyptian hieroglyph.</td>
</tr>
</tbody>
</table>

Table 4.9. A possible analogy between the decoding of Egyptian hieroglyphs and the human genome. (Reproduced from S. Ji, Cell Language Theory, World Scientific, 2017)

<table>
<thead>
<tr>
<th>Egyptian Hieroglyphs</th>
<th>Human Genome</th>
<th>A</th>
<th>B</th>
<th>C</th>
</tr>
</thead>
<tbody>
<tr>
<td>Logograms</td>
<td>Genetic Information</td>
<td>Information</td>
<td>Information-energy (or Gnergy) whose discrete units being conformons</td>
<td>Logophonograms</td>
</tr>
</tbody>
</table>
Table 4.10. A comparison between Egyptian hieroglyphs and DNA texts. (Reproduced from S. Ji, Cell Language Theory, World Scientific, 2017)

<table>
<thead>
<tr>
<th></th>
<th>Egyptian Hieroglyphs</th>
<th>DNA Molecular Text</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Embodied in</td>
<td>Rosetta Stone</td>
<td>Human brain</td>
</tr>
<tr>
<td>2. Known glyphs</td>
<td>Greek and Demotic</td>
<td>Human language</td>
</tr>
<tr>
<td>3. Unknown glyphs</td>
<td>Old Egyptian</td>
<td>Cell language</td>
</tr>
<tr>
<td>4. Semantic</td>
<td>Decree of Memphis</td>
<td>Isomorphism between cell and human language</td>
</tr>
<tr>
<td>connection</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5. Key to decoding</td>
<td>‘Logophonogram’</td>
<td>Conformons</td>
</tr>
</tbody>
</table>
What is the Conformon?

- **Conformons** are packets of mechanical energy (also called conformational energy) stored in biopolymers (i.e., proteins, RNA & DNA). Conformations are 3-D structures of molecules that can be changed without making or breaking covalent bonds.

- Because **conformons** are localized in sequence-specific sites within biopolymers, they carry both free energy (due to mechanical strains) and genetic information (due to sequence-specificity).

- Therefore, biopolymers harboring **conformons** can generate mechanical forces (due to free energy) oriented in a specific direction (due to genetic information) in order to cause goal-directed motions on their environment, including bound substrates, ligands, and ions.

- Enzymes can use **conformons** to modulate the activation energy barriers so as to increase or even decrease the rate of chemical reactions they catalyze.
The History of Conformons

The definition: Conformon = conform- (meaning conformation of biopolymers) + -on (meaning discrete entities)

1972: Conformational strains of biopolymers that carry free energy to drive molecular processes in mitochondria (D. E. Green & S. Ji, 1972)

1983: Sequence-specific conformational strains of biopolymers that carry free energy (to do work) and genetic information (to control work) that are necessary and sufficient to drive all goal-oriented molecular processes inside the cell (Ji, 1974, 1985).

1991: C. Benham (1992) invoked a similar idea independently which he called SIDDs (stress-induced duplex destabilization). SIDDs are direct experimental evidence for conformons.

2007: Single-molecule measurements on enzymes and molecular motors demonstrate that mechanical energies (i.e., conformons) are indeed stored in proteins (Ishii and Yanagida, 2007)

2008: PDE (Planckian Distribution Equation) fits the single-molecule enzyme kinetic data of cholesterol oxidase (measured by Lu, Xun and Xie, 1998), indicating that standing waves generated inside enzymes may play a fundamental role in enzyme catalysis (Ji, 2008, 2012, 2017).
What Do Conformons Do in the Cell?

- The cell can be viewed as a system of molecular machines.
- Like artificial machines, molecular machines need free energy to generate forces inside them.
- Molecular machines are enzymes that catalyze exergonic chemical reactions to generate conformons within themselves.
- Conformons provide the immediate free energy to generate forces within molecular machines.
- Molecular machines exert forces on their environment to perform work on it, including gene expression, active transport, muscle contraction, and cell motility.
DNA Supercoils as Evidence for Conformons

The relaxed (b) and supercoiled (a) conformations of DNA:
Supercoiled DNA stores mechanical strains (also called mechanical energy) at sequence-specific sites (i.e., *conformons* !) as can be demonstrated by experiments as well as by computer simulations [11].

Visualization of Circular DNA Molecules Having Different Linking Numbers (i.e., Supercoils or Conformons)

Figure 31-18
Gel patterns showing the relaxation of supercoiled SV40 viral DNA. Part A is a highly negatively supercoiled DNA. Incubation of the DNA with a topoisomerase for (B) 5 minutes and (C) 30 minutes leads to a series of bands that have less supercoiling. The $Lk$ values of adjacent bands differ by 1, and average $Wr$ values by about 0.7.


(Stryer, 1995, p. 797)
**Linking Deficiency, \( \alpha \), as a Quantitative Measure of Conformons**

White’s formula is a mathematical equation stating that the linking number, \( L_k \) (the number of times the two strands are intertwined while the helical axis is kept on a plane), can be partitioned into twist, \( T_w \) (a number determined by the local pitch of the helix, regardless of the configuration of the helical axis), and writhe, \( W_r \) (a number determined by the degree of the contortion of the helical axis in space).

\[
L_k = T_w + W_r
\]

\[
\alpha = \Delta T_w + \Delta W_r
\]

Inside the cell, DNA molecules are commonly maintained by topoisomerases in negatively supercoiled states, making their linking number \( L_k \) smaller than their relaxed values, \( L_{k0} \). *The linking number deficiency, \( L_k - L_{k0} < 0 \), is often denoted as \( \alpha \), which can be expressed as shown above. \( \alpha \) is a quantitative measure of conformons embedded in circular DNA.* [C. J. Benham, CABIOS 12 (5):375-381 (1996)]
Conformons and Life: The Conformon Theory of Life

(1) The cell is the unit of life.

(2) The cell is an organized system of molecular machines [18], biopolymers that carry out molecular work processes (such as simple catalysis, active transport, muscle contraction, gene expression, and DNA repair).

(3) Molecular machines are driven by forces generated from conformons.

(4) Conformons are packets of mechanical energy derived from chemical reactions and stored in sequence-specific sites within biopolymers.

(5) Therefore, life is ultimately driven by chemical reactions mediated by conformons:

Conformons

CHEMICAL REACTIONS  ------------------> LIFE
**Blackbody radiation equation:**

\[ u(\lambda, T) = \frac{(2hc^2/\lambda^5)}{(e^{hc/\lambda kT} - 1)} \]  \hspace{1cm} (1)

**Blackbody radiation-like equation (BRE)**

\[ y = \frac{a}{x^5}/(e^{b/x} - 1) \]  \hspace{1cm} (2)

**Planckian Distribution Equation (PDE)**

\[ y = \frac{A}{(x + B)^5}/(e^{C/(x + B)} - 1) \]  \hspace{1cm} (3)
Evidence for the role of the Wave-Particle Complementarity in molecular and cell biology

Enzyme Catalysis

Cholesterol oxidase molecule

Cell Metabolism

Budding yeast cells

PDE

(Planckian Distribution Equation)

Number of standing waves per unit frequency per unit volume

Average energy per standing wave

\[ y = \frac{A}{(x + B)^5} \cdot \frac{1}{e^{C/(x + B)} - 1} \]
Quantization of Energy Levels in Atoms and Enzymes
The *Chladni Patterns*: Visualizing the **Standing Wave-Energy Relation of the PDE** (Planckian Distribution Equation)

**Figure 4.13.** Formation of the standing waves of particles (also called Chladni figures) on a metal plate vibrating at increasing frequencies, top to bottom. Retrieved from [https://en.wikipedia.org/wiki/Ernst_Chladni](https://en.wikipedia.org/wiki/Ernst_Chladni) and [https://www.youtube.com/watch?v=wMIvAsZvBiw](https://www.youtube.com/watch?v=wMIvAsZvBiw). Reviewed in [723].
Mathematics and Physics of Waves

a  Fourier Theorem

b  Standing waves

c  Resonance
Whenever a long tailed histogram fits PDE, it may be concluded that a wave-particle duality principle is implicated in the physicochemical process (called the Planckian process) that generated the numbers underlying the histogram fitting PDE.
The Petoukhov Hypothesis: 
Organisms are musical instruments

Sergey Petoukhov [16]

"Living bodies possess innate ability to use acoustic resonances, reproduce resonant frequencies of speech, singing and musical instruments, and use resonances as carriers of information."

“Any living organism is a great chorus of coordinated oscillatory processes (mechanical, electrical, piezoelectric, biochemical, etc.), which are connected with their genetic inheritance along chains of generations. Since ancient times, chrono-medicine believes that all diseases are the result of disturbances in the ordered set of oscillatory processes.”

“Any living body is a musical instrument (a synthesizer with an abundance of rearrangements of resonant modes).”
“The CymaScope is a new type of scientific instrument that makes sound visible. . . . The surface tension of water has high flexibility and fast response to imposed vibrations, even with transients as short-lived as a few milliseconds. Therefore, water is able to translate many of the sinusoidal periodicities—in a given sound sample—into physical wavelet structures on the water’s surface and subsurface. Current limits to imprinting sound on water occur in the higher harmonics and are due mainly to there being insufficient energy available in this area of the audio spectrum to cause excursions of the surface tension membrane.” Retrieved from https://www.cymascope.com/cymascope.html

Figure 4.14. Music visualized using a CymaScope. (A) Female vocal sounds. (B) 12 piano notes. All these images were retrieved from https://www.cymascope.com/shop/cymaart-prints/ or http://www.cymascope.com/cyma_research/musicology.html on 10/11/2016.

The cell images were obtained with the digital CymaScope [12-14] in 2017 in collaboration with Ryan Stables [15] and John S. Reid [12] with the financial support from GreenMedInfo. I thank Mr. Beum Jun Park for performing the nonlinear fitting of the histograms to PDE. (Warning: The apparent difference between the two images shown below may not be statistically significant due to extreme heterogeneities of CymaGlyphs. Further research is in progress.)

#31

Healthy cell  
Cancer cell

CymaScopic images (i.e., CymaGlyphs) of the audio files generated from sonifying Raman spectra of single cells

The fitting to PDE (red) of the histograms (blue) generated from the digitized CymaGlyphs
Conclusions

(1) DNA and genes are not passive carriers of information but active executioners of genetic information driven by conformons carried by enzymes.

(2) Enzymes carry genetic information in their monomer sequences and mechanical energy in their conformational strains.

(3) There are two kinds of molecular machines – active and passive. DNA and genes are passive molecular machines driven by enzymes which are active molecular machines.

(4) Therefore DNA carries not just genetic information (as widely believed) but also mechanical energy, i.e., DNA carries conformons.

(5) Decoding DNA may be akin to the decoding of the Rosetta Stone: i.e., DNA may be the molecular Rosetta Stone.

(6) The living cell, as a system of molecular machines (Alberts et al., Molecular Biology of the Cell, 2008), is the only material system that can read and execute the genetic instructions encoded in DNA.

(7) To understand how genes work, it is absolutely necessary to understand how enzymes and cells work on the molecular level.

(8) Molecular machines obey the physical principle of wave-particle duality and the mathematical principle of the Fourier theorem.

(9) The paradigm shift from classical genetics of the past centuries to a new genetics of the 21st century based on semiotics and the principle of wave-particle duality or complementarity is urgently needed.