Robustness

*from Wikipedia*: "Robustness is the quality of being able to withstand stresses, pressures, or changes in procedure or circumstance. A system, organism or design may be said to be "robust" if it is capable of coping well with variations (sometimes unpredictable variations) in its operating environment with minimal damage, alteration or loss of functionality."

1) Redundancy
2) “Compartmentation”/ Modularity
3) Weak linkage
4) Exploratory mechanisms / Plasticity
5) Feedback
6) Degeneracy

Kirschner & Gerhart 1998
Robustness and “Evolvability”

Gerhart & Kirschner, “Cells, Embryos, and Evolution” 1997
Redundancy
“Exon shuffling” was recognized early in molecular biology as a potential mechanism to generate diverse novel proteins based on existing functional building-blocks.
Weak Linkage

Chalmers et al. 2007
Modularity + Redundancy

Maternal morphogen gradients
e.g. nanos
bicoid

Gap genes
e.g. Kruppel

Pair-rule genes
e.g. even-skipped

Segment polarity genes
e.g. engrailed
wingless

Hox genes
e.g. Ultrabithorax
abdominal A

Thorax

Abdomen
Evolvability
Modularity

“Hypercolumn”

after Hubel & Wiesel 1962
Weak Linkage

layer 2/3
P3C2.E20/87 S18

layer 5/6
P5C6.E21 S22

20 mV
100 ms

Douglas & Martin 1991
Modularity + Weak Linkage
Modularity combined with weak linkage promotes computational flexibility and ensures that the system “fails gracefully.”

Ponce et al. 2008
computational complementarity
Exploratory Mechanisms

- exploration
- competition
- self-assembly
Exploratory Mechanisms: Competition

Competitive synaptic interactions at the developing neuromuscular junction

Learning: The ultimate exploratory mechanism

Steve Lisberger
Modularity combined with plasticity may permit an organism to process a new input without evolving an entirely novel circuit from scratch—in effect, building diverse novel brains using existing building-blocks.

Sur et al. 1988
Evolvability

Because circuits can wire themselves up and learn about regularities in their inputs, changes in the periphery can, to a certain extent, be automatically incorporated into behaviors.

Smallwood et al. 2003

Jacobs et al. 2007
1. Homeostatic plasticity: slow feedback for robustness

2. Degeneracy in neuron and network function

3. Sensory feedback in the fly visual system and its modulation by flight
Robustness ≈ stability
We can think about stability of neuron function in the face of turnover, growth, learning.

Synaptic Scaling is an example of Homeostatic Plasticity
Synaptic scaling – rat visual cortical neurons in culture grown with TTX or bicuculline

Turrigiano GG et al 1998
Synaptic scaling – rat visual cortical neurons in culture grown with TTX or bicuculline

Turrigiano GG et al 1998
Other examples of homeostatic plasticity – intrinsic conductances

B

Day 2

V

I

Day 3

V

I

A

Control

Stimulation

Reversal

15 mV
1 nA
1 s

20 mV
0.5 s

Turrigiano Abbott and Marder 1994
Homeostatic negative feedback
Gives your system robustness
Robustness:
The ability of a system to perform consistently under a variety of conditions

1. Homeostatic plasticity: slow feedback for robustness
2. Degeneracy in neuron and network function
3. Sensory feedback in the fly visual system and its modulation by flight
**degeneracy** – the condition of having multiple distinct mechanisms for reaching the same outcome

this is distinct from

**redundancy** – the condition of having multiple copies of the same mechanism
A classic example of degeneracy in biology: the genetic code

<p>| | | |</p>
<table>
<thead>
<tr>
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<tbody>
<tr>
<td><strong>Ala/A</strong></td>
<td>GCU, GCC, GCA, GCG</td>
<td><strong>Leu/L</strong></td>
</tr>
<tr>
<td><strong>Arg/R</strong></td>
<td>CGU, CGC, CGA, CGG, AGA, AGG</td>
<td><strong>Lys/K</strong></td>
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<tr>
<td><strong>Asn/N</strong></td>
<td>AAU, AAC</td>
<td><strong>Met/M</strong></td>
</tr>
<tr>
<td><strong>Asp/D</strong></td>
<td>GAU, GAC</td>
<td><strong>Phe/F</strong></td>
</tr>
<tr>
<td><strong>Cys/C</strong></td>
<td>UGU,UGC</td>
<td><strong>Pro/P</strong></td>
</tr>
<tr>
<td><strong>Gln/Q</strong></td>
<td>CAA, CAG</td>
<td><strong>Ser/S</strong></td>
</tr>
<tr>
<td><strong>Glu/E</strong></td>
<td>GAA, GAG</td>
<td><strong>Thr/T</strong></td>
</tr>
<tr>
<td><strong>Gly/G</strong></td>
<td>GGU, GGC, GGA, GGG</td>
<td><strong>Trp/W</strong></td>
</tr>
<tr>
<td><strong>His/H</strong></td>
<td>CAU, CAC</td>
<td><strong>Tyr/Y</strong></td>
</tr>
<tr>
<td><strong>Ile/I</strong></td>
<td>AUU, AUC, AUA</td>
<td><strong>Val/V</strong></td>
</tr>
<tr>
<td><strong>START</strong></td>
<td>AUG</td>
<td><strong>STOP</strong></td>
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Because multiple codes can specify the same amino acid, the genetic code is said to be degenerate.
System Variables

- Intrinsic conductances
- Synaptic conductances
- Modulatory inputs

System outputs

- Firing patterns – bursting/tonic/adapting
- Input / output functions – gain
- Plateau properties – bi-/multi-stability

Diagram:
- Input → System variables → Output
- Homeostat
- Set point
This is a physiologically identified crab neuron that does the same thing in all crabs.

Marder and Goaillard 2006
Individual intrinsic currents vary 2-4 fold from animal to animal.
Burst firing in Purkinje Neurons: a stereotyped neuronal behavior where we can carefully measure underlying system variables.
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Swensen and Bean 2005
Mapping parameter space for individual neurons
Mapping parameter space for individual neurons
Burst firing in Purkinje Neurons: a stereotyped neuronal behavior where we can carefully measure underlying system variables.

Swensen and Bean 2005
Neuron-level degeneracy: predicting compensatory relationships

A

![Graph showing relative current vs. [TTX] (nM)]

B

![Graph showing voltage recordings with different TTX concentrations]

Swensen & Bean, J. Neurosci. 2005
An acute decrease in Na\(^+\) conductance produces a compensatory increase in voltage-dependent and Ca\(^{2+}\)-dependent K\(^+\) conductances.

Swensen & Bean, J. Neurosci. 2005
Neuron-level degeneracy: long-term compensatory relationships

Swensen & Bean, J. Neurosci. 2005
Neuron-level degeneracy: predicting compensatory relationships

A chronic decrease in Na$^+$ conductance produces a compensatory increase in Ca$^{2+}$ conductance.
In this example,
• membrane potential is the robust system output
• a fast feedback loop is created by voltage-dependent and Ca^{2+}-dependent K^{+} channels
• a slow feedback loop regulates Ca^{2+} conductances
• many combinations of conductances (i.e., “system variables”) can produce similar output
Circuit-level degeneracy: robustness of patterns in the stomastogastric ganglion

the pyloric network

<table>
<thead>
<tr>
<th>AB/PD</th>
<th>LP</th>
<th>PY</th>
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Fast glutamatergic
Slow cholinergic

note: all synapses are inhibitory

the pyloric rhythm

PD
LP
PY
Circuit-level degeneracy: similar network activity from disparate cellular and synaptic parameters

model neurons of pyloric network
Degeneracy

• permits tolerance to many kinds of perturbations
• while also maintaining sensitivity to other sorts of perturbations

Degeneracy also allows a population to harbor latent diversity, potentially creating diverse avenues for evolution or modulation.