



**NANYANG**  
TECHNOLOGICAL  
UNIVERSITY



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## Asymmetry of Genetic Code and the Role of Parrondo's Paradox

*presented by*

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*B.Eng. MAE, NTU 2011*

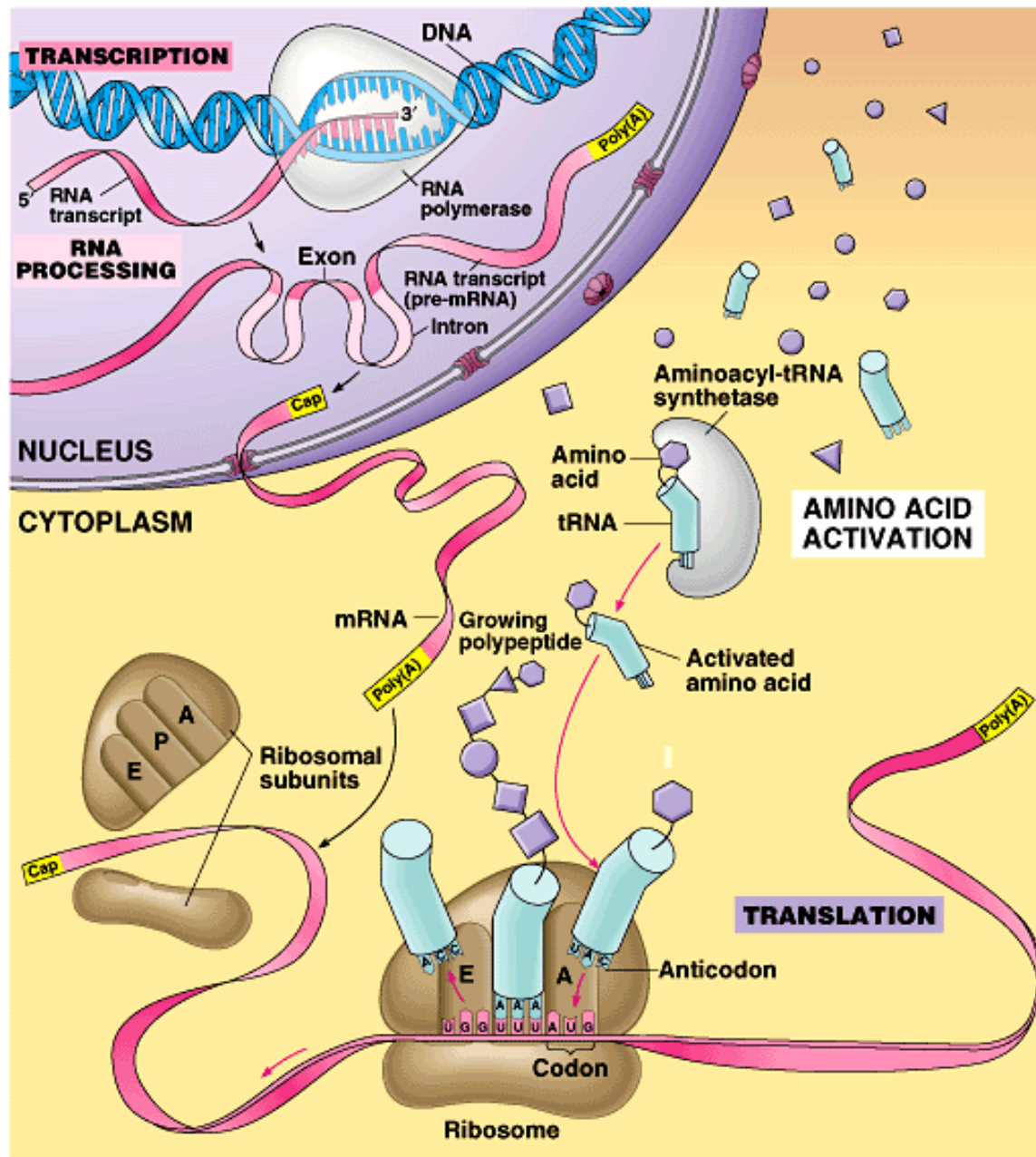
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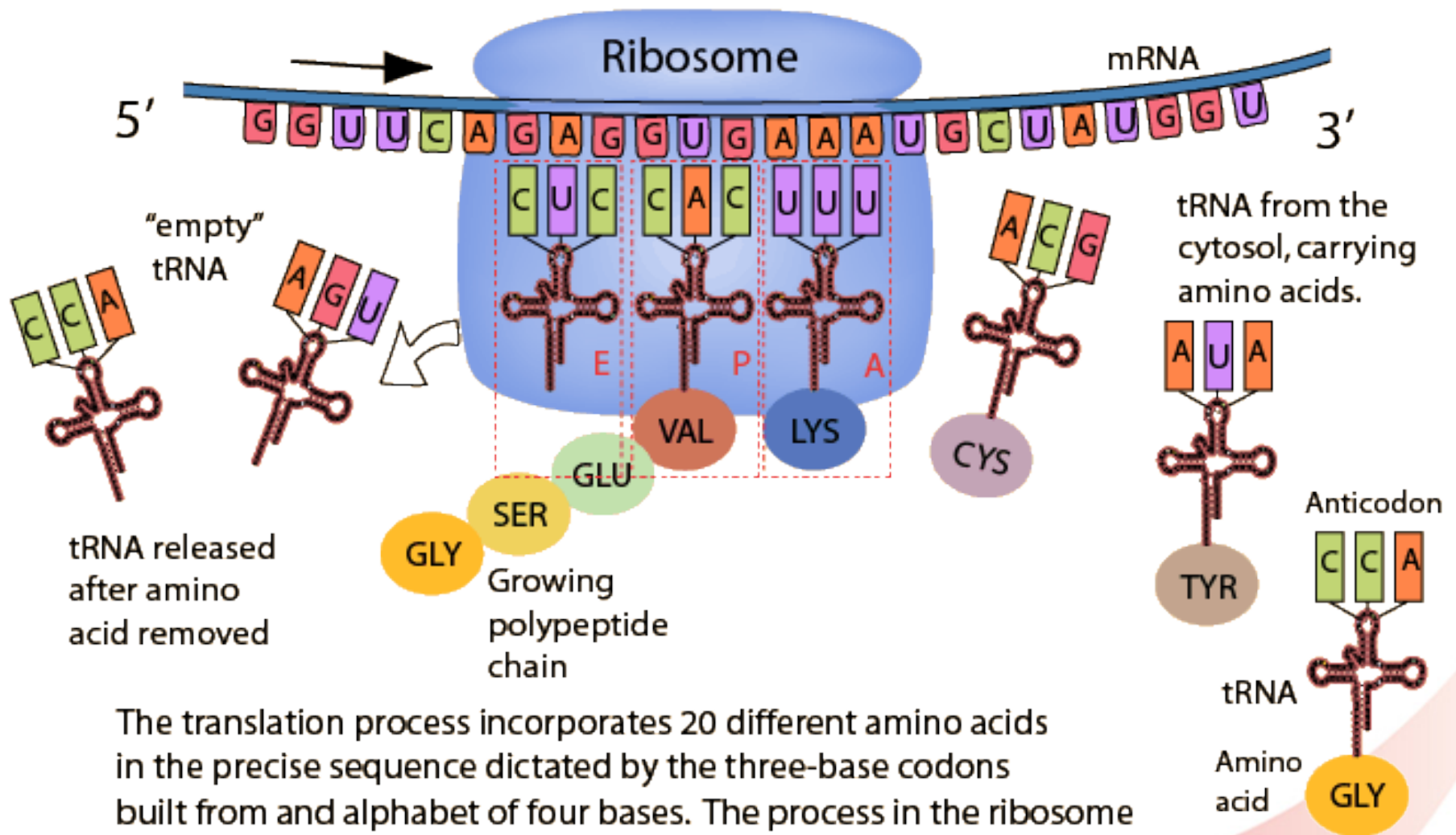
*14 July 2015, Barcelona, Spain*

# Introduction to Genetic Code

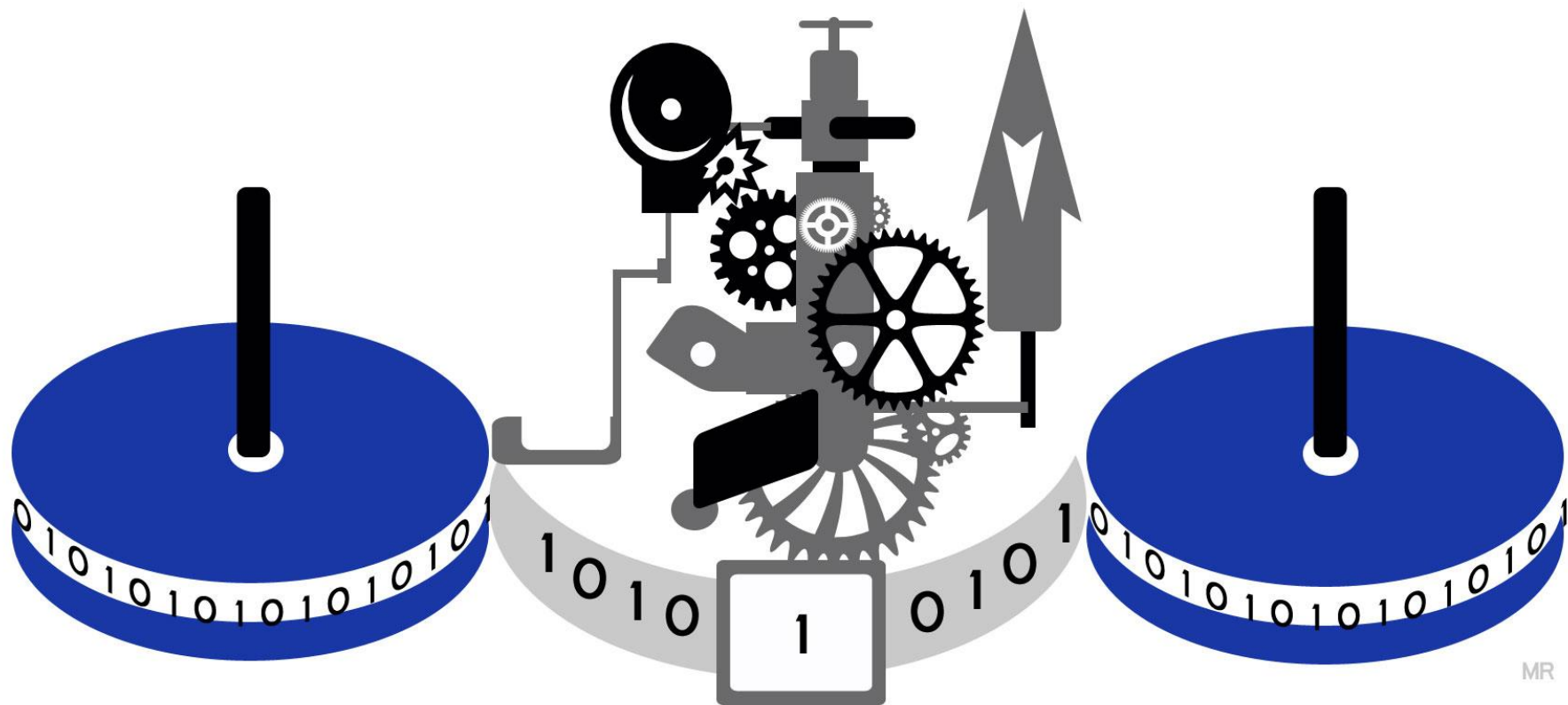
- Protein – essential component of living beings
- How is protein synthesized?



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The translation process incorporates 20 different amino acids in the precise sequence dictated by the three-base codons built from an alphabet of four bases. The process in the ribosome builds the polypeptide chains that will become proteins.



MR

# Introduction to Genetic Code

- The rule that determine what sequence produce which amino acids
- 3 nucleotides triplets/letters codon
- Code for 20 standard amino acids
- 4 types of nucleotides: ATCG (DNA), AUCG (RNA)

# Standard Genetic Code

- First letter: Similar biosynthesis process
- Second letter: Similar Chemical properties (polarity, acidity/basicity, etc.)
- Third letter: Redundancy?

# Standard Genetic Code

1st base	2nd base								3rd bases
	U		C		A		G		
U	UUU	Phenylalanine	UCU	Serine	UAU	Tyrosine	UGU	Cysteine	U
	UUC	Phenylalanine	UCC	Serine	UAC	Tyrosine	UGC	Cysteine	C
	UUA	Leucine	UCA	Serine	UAA	Stop	UGA	Stop	A
	UUG	Leucine	UCG	Serine	UAG	Stop	UGG	Tryptophan	G
C	CUU	Leucine	CCU	Proline	CAU	Histidine	CGU	Arginine	U
	CUC	Leucine	CCC	Proline	CAC	Histidine	CGC	Arginine	C
	CUA	Leucine	CCA	Proline	CAA	Glutamine	CGA	Arginine	A
	CUG	Leucine	CCG	Proline	CAG	Glutamine	CGG	Arginine	G
A	AUU	Isoleucine	ACU	Threonine	AAU	Asparagine	AGU	Serine	U
	AUC	Isoleucine	ACC	Threonine	AAC	Asparagine	AGC	Serine	C
	AUA	Isoleucine	ACA	Threonine	AAA	Lysine	AGA	Arginine	A
	AUG	Methionine	ACG	Threonine	AAG	Lysine	AGG	Arginine	G
G	GUU	Valine	GCU	Alanine	GAU	Aspartic acid	GGU	Glycine	U
	GUC	Valine	GCC	Alanine	GAC	Aspartic acid	GGC	Glycine	C
	GUA	Valine	GCA	Alanine	GAA	Glutamic acid	GGA	Glycine	A
	GUG	Valine	GCG	Alanine	GAG	Glutamic acid	GGG	Glycine	G

Nonpolar
polar
basic
acidic
Stop



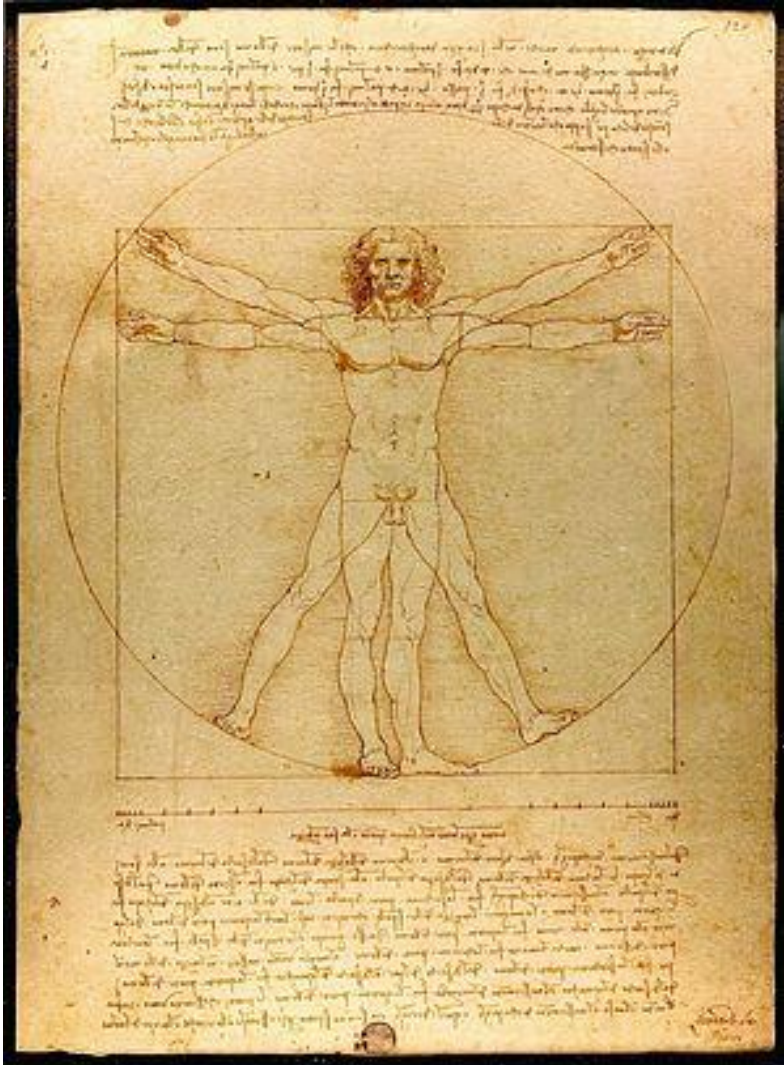
# Restructured Genetic Code

1st base	3rd base								2nd bases
	U		A		G		C		
U	UUU	Phenylalanine	UUA	Leucine	UUG	Leucine	UUC	Phenylalanine	U
	UAU	Tyrosine	UAA	Stop	UAG	Stop	UAC	Tyrosine	A
	UGU	Cysteine	UGA	Stop	UGG	Tryptophan	UGC	Cysteine	G
	UCU	Serine	UCA	Serine	UCG	Serine	UCC	Serine	C
A	AUU	Isoleucine	AUA	Isoleucine	AUG	Methionine/start	AUC	Isoleucine	U
	AAU	Asparagine	AAA	Lysine	AAG	Lysine	AAC	Asparagine	A
	AGU	Serine	AGA	Arginine	AGG	Arginine	AGC	Serine	G
	ACU	Threonine	ACA	Threonine	ACG	Threonine	ACC	Threonine	C
G	GUU	Valine	GUA	Valine	GUG	Valine	GUC	Valine	U
	GAU	Aspartic acid	GAA	Glutamic acid	GAG	Glutamic acid	GAC	Aspartic acid	A
	GGU	Glycine	GGA	Glycine	GGG	Glycine	GGC	Glycine	G
	GCU	Alanine	GCA	Alanine	GCG	Alanine	GCC	Alanine	C
C	CUU	Leucine	CUA	Leucine	CUG	Leucine	CUC	Leucine	U
	CAU	Histidine	CAA	Glutamine	CAG	Glutamine	CAC	Histidine	A
	CGU	Arginine	CGA	Arginine	CGG	Arginine	CGC	Arginine	G
	CCU	Proline	CCA	Proline	CCG	Proline	CCC	Proline	C

# Human body



# Leonardo's Vitruvian Man



- “Symbol of essential symmetry of the human body, and by extension, of the universe as a whole”

# Asymmetrical Region

UAA	<b>Stop</b>	UAG	<b>Stop</b>
UGA	<b>Stop</b>	UGG	<b>Tryptophan</b>
UCA	<b>Serine</b>	UCG	<b>Serine</b>
AUA	<b>Isoleucine</b>	AUG	<b>Methionine/start</b>

# Methionine and Tryptophan

- Dietary restriction of Methionine and Tryptophan extends lifespans

Miller, R.A., et al., *Aging Cell*, vol. 4, no. 3, pp. 119-125, 2005.

Komninou, D., et al., *Nutrition and Cancer*, vol. 54, no. 2, pp. 202-208, 2006.

Grandison, R.C., et al., *Nature*, vol. 462, no. 7276, pp. 1061-1064, 2010.

M. B. C. & K. B. Kaeberlein, *PLoS Genetics*, vol. 3, no. 5, p. e84, 2007.

Piper, M.D. & Bartke, A., *Cell Metabolism*, vol. 8, no. 2, p. 99, 2008.

Colman, R.J., et al., *Science*, vol. 325, no. 5937, p. 201, 2009.

De Marte, M.L. & Enesco, H.E., *Mechanisms of Ageing and Development*, vol. 36, no. 2, p. 161, 1986.

Zimmerman, J.A., et al., *Experimental Gerontology*, vol. 38, no. 1-2, pp. 47-52, 2003.

- DR lowers fecundity as well

Partridge, L., et al., *Cell*, vol. 120, no. 4, pp. 461-472, 2005.

M. Klass, *Mechanisms of Ageing and Development*, vol. 6, no. 6, pp. 413-429, 1977.

Chapman, T. & Partridge, L., *Proceedings: Biological Sciences*, vol. 263, no. 1371, pp. 755-759, 1996.

Selesniemi, K., et al., *Aging Cell*, vol. 7, no. 5, pp. 622-629, 2008.

# Survival vs Reproduction

- Dietary restriction – evolve response to food shortage in nature
- Limited resources reserved for most important operation during shortage
- Resources allocated to ensure survivability while reproduction withheld

Harrison, D.E. & Archer, J.R., *Growth, Development, and Aging*, vol. 53, no. 1-2, p. 3, 1989.

R. Holliday, *Bioessays*, vol. 10, no. 4, pp. 125-127, 1989.

G. Williams, *The American Naturalist*, vol. 100, no. 916, pp. 687-690, 1966.

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Mair, W. & Dillin, A., *Annual Review of Biochemistry*, vol. 77, pp. 727-754, 2008.

- Time of scarcity
  - Not enough food for both parents and offspring
  - Consume resources and endanger parents
  - Survive and wait for a better future
- Time of abundant
  - Enough resources for both parents and offspring
  - Pass down on gene to next generation

# Asymmetrical Region

UAA	Stop	UAG	Stop
UGA	Stop	UGG	Tryptophan
UCA	Serine	UCG	Serine
AUA	Isoleucine	AUG	Methionine/start

- With the function of Tryptophan and Methionine in the asymmetrical structure, Parrondo's effect can play a role



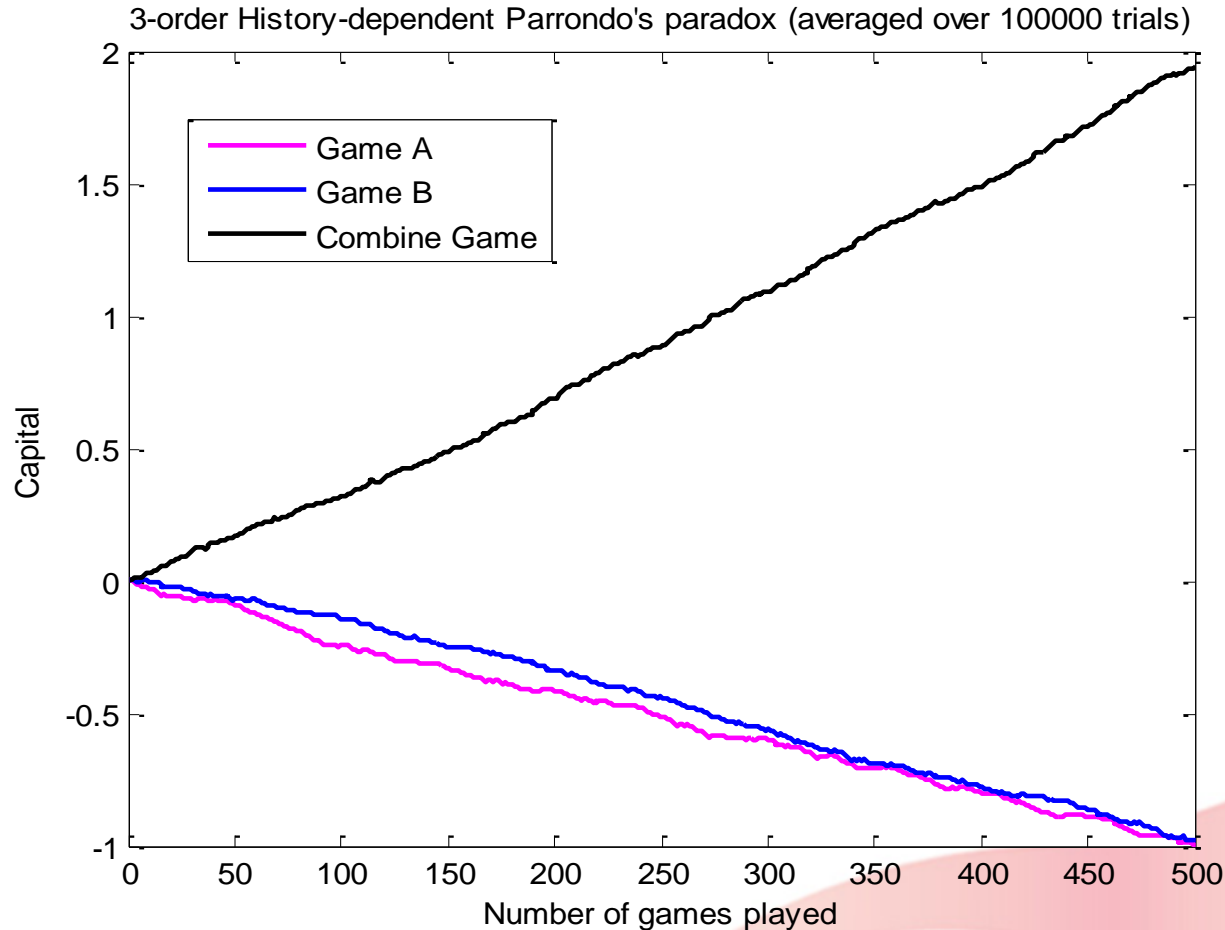
# 3<sup>rd</sup> Order Path Dependent Parrondo's Paradox

- Game A – random game
- Game B – Path dependent game
- Game B depend on results of previous 3 games

# Game B

State	Result of game at ( $t - 3$ )	Result of game at ( $t - 2$ )	Result of game at ( $t - 1$ )	Probability of Win
1	Loss	Loss	Loss	$p_1$
2	Loss	Loss	Win	$p_2$
3	Loss	Win	Loss	$p_3$
4	Loss	Win	Win	$p_4$
5	Win	Loss	Loss	$p_5$
6	Win	Loss	Win	$p_6$
7	Win	Win	Loss	$p_7$
8	Win	Win	Win	$p_8$

# 3<sup>rd</sup> Order Path Dependent Parrondo's Paradox



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	AGU	Serine	AGA	Arginine	AGG	Arginine	AGC	Serine	G
	ACU	Threonine	ACA	Threonine	ACG	Threonine	ACC	Threonine	C
G	GUU	Valine	GUA	Valine	GUG	Valine	GUC	Valine	U
	GAU	Aspartic acid	GAA	Glutamic acid	GAG	Glutamic acid	GAC	Aspartic acid	A
	GGU	Glycine	GGA	Glycine	GGG	Glycine	GGC	Glycine	G
	GCU	Alanine	GCA	Alanine	GCG	Alanine	GCC	Alanine	C
C	CUU	Leucine	CUA	Leucine	CUG	Leucine	CUC	Leucine	U
	CAU	Histidine	CAA	Glutamine	CAG	Glutamine	CAC	Histidine	A
	CGU	Arginine	CGA	Arginine	CGG	Arginine	CGC	Arginine	G
	CCU	Proline	CCA	Proline	CCG	Proline	CCC	Proline	C

# Analogy

- Noise from surrounding – analogous to game A
- Expression of amino acids ‘left’ and ‘right’ from three nucleotides – analogous to game B

# Natural Switch

- Mechanism biased towards the expression of the G-C side (Methionine-Tryptophan)
- During stable period, no noise, reproduce and pass down gene to next generation
- Offspring has higher chance of surviving
- Pure game B

- During turbulent and unstable period, more noise, reproduction stop and life extended
- Reproduction endanger offspring and parents
- Game B + game A = compound game

- Correct action taken by species can determine life/death, extinction/dominance
- Genetic code structure with the embedded asymmetry region and Parrondo's effect enable such switch of action to happen



# Conclusion

- Restructured genetic code – Asymmetry embedded in general symmetry.
- What is the purposed?
- As a switch using Parrondo's effect?

Thank you for you time