A novel mathematical tool for generating highly conserved protein domain via different organismal genomic landscapes

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Darwinian evolution hypothesizes that a short stretch of DNA was first constructed and then it expanded to give rise to a long strand. This long strand then produced a mix of exons, introns and repetitive DNA sequence. The order of production of above three kinds of DNA sequence is unknown. Reshuffling of stretches of DNA like above within organisms has given rise to different chromosomes. Till date it is not known how this process is governed. In this paper we show that starting with a sixteen base-pair human olfactory DNA sequence one can form a highly conserved protein domain. Once this domain is formed repetitive DNA sequences of a particular kind starts generating which signifies that this particular conserved protein domain will be unique in nature. The entire mathematical exercise presented in this paper is based on simplest possible context free L-System which we think has been adopted by biological system in general.

Context free L-System [1, 2, 3, 4], considered to be one of simplest, originally proposed by Hungarian Biologist A. Lindenmayer [5] to study symmetry of plants can be used to generate a large length of DNA sequence with a definite size limit. We took a human olfactory receptor DNA sequence (OR1F1) and derived an L-System with following production rule [(Axiom: A) A ATGA, C GCGG, T GACA, G AACC] which basically covers extreme 5'-end of OR1F1. 1024 bp length DNA sequence [Fig. 1] generated from this production rule showed 3 Open Reading Frames (ORF) in 3' 5' direction [Fig. 2].

Fig.1

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ATGAGACAAACCATGAAACCATGAGCGGATGAATGAATGAGCGGGCGGATGAGACAAACCATGAATGAATGAGCGGGCGGATGAGACAAACCATGAAACCGCGGAACCAAC
CATGAGACAAACCATGAATGAGACAAACCATGAATGAGACAAACCATGAAACCGCGGAACCAACCAACCGCGGAACCAACCATGAGACAAACCATGAAACCATGAGCGGAT
GAATGAATGAGCGGGCGGATGAGACAAACCATGAATGAGACAAACCATGAATGAGACAAACCATGAAACCGCGGAACCAACCAACCGCGGAACCAACCATGAGACAAACCA
TGAAACCATGAGCGGATGAATGAATGAGCGGGCGGATGAGACAAACCATGAATGAATGAGCGGGCGGAACCGCGGAACCAACCATGAATGAGCGGGCGGATGAATGAGCGG
GCGGATGAGACAAACCATGAAACCATGAGCGGATGAATGAATGAGCGGGCGGATGAGACAAACCATGAATGAGACAAACCATGAAACCATGAGCGGATGAATGAATGAGCG
GGCGGATGAGACAAACCATGAATGAGACAAACCATGAAACCATGAGCGGATGAATGAATGAGCGGGCGGATGAGACAAACCATGAATGAATGAGCGGGCGGAACCGCGGA
CCAACCATGAATGAGCGGGCGGATGAATGAGCGGGCGGATGAATGAGCGGGCGGAACCGCGGAACCAACCATGAATGAGCGGGCGGATGAATGAGCGGGCGGATGAGACAA
ACCATGAAACCATGAGCGGATGAATGAATGAGCGGGCGGATGAGACAAACCATGAATGAATGAGCGGGCGGATGAGACAAACCATGAAACCGCGGAACCAACCATGAGACA
AACCATGAATGAGACAAACCATGAATGAGACAAACCATGAAACCGCGGAACCAACCAACCGCGGAACCAACCATGAGACAAACCATGAAACCATGAGCGGATGAATGAATG
AGCGGGCGGATGAGACAAACCATGA
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Fig.3 Legend. The complementary strand of Fig.1 in the 5' 3' direction.

This sequence when conceptually translated and it gave rise to three ORFs in 5' 3' direction (Fig.4).

Fig.4

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5'3' Frame 1
Y S V W Y F G T R L L T Y S P A Y S V W Y L L T R P P T L F G T L A P W L V L C L V L T L F G T Y S V W Y F G
A L V G W R L G W Y S V W Y F G T R L L T Y S P A Y S V W Y L L C L V L T L F G T L A P W L V G A L V G T L F
G T L V L A Y L L T R P P T L F G T Y L L A R L L C L V L W Y S P T Y L L A R
L L C L V L T L F G T L V L A Y L L T R P P T L F G T Y S V W Y F G T R L L T Y S P A Y S V W Y L L T R P P W
R L G W Y L L A R L L T R P P T Y S P A L A P W L V L T R P P T Y S P A Y S V W Y F G T R L L T Y S P A Y S V
W Y L L T R P P T L F G T L A P W L V L C L V L T L F G T Y S V W Y F G A L V G W R L G W Y S V W Y F G T R L
L T Y S P A Y S V W Y

5'3' Frame 2
T L F G T L V L A Y L L T R P P T L F G T Y L L A R L L C L V L W R L G W Y S V W Y L L C L V L T L F G T L A
P W L V G A L V G T L F G T L V L A Y L L T R P P T L F G T Y S V W Y L L C L V L W R L G W L A P W L V L C L
V L W Y S P T Y L L A R L L C L V L T Y S P A L A P W L V L T R P P T Y S P A Y S V W Y F G T R L L T Y S P A
Y S V W Y L L C L V L W Y S P T Y L L A R L L C L V L T L F G T L V L A Y L L T R P P T L F G T Y L L A R L G
A L V G T Y S P A Y L L A R L L T R P P W R L G W Y L L A R L L T R P P T L F G T L V L A Y L L T R P P T L F
G T Y L L A R L L C L V L W R L G W Y S V W Y L L C L V L T L F G T L A P W L V G A L V G T L F G T L V L A Y
L L T R P P T L F G T

5'3' Frame 3
L C L V L W Y S P T Y L L A R L L C L V L T Y S P A Y S V W Y F G A L V G T L F G T Y S V W Y L L C L V L W R
L G W L A P W L V L C L V L W Y S P T Y L L A R L L C L V L T L F G T Y S V W Y F G A L V G W R L G W Y S V W
Y F G T R L L T Y S P A Y S V W Y L L T R P P W R L G W Y L L A R L L T R P P T L F G T L V L A Y L L T R P P
T L F G T Y S V W Y F G T R L L T Y S P A Y S V W Y L L C L V L W Y S P T Y L L A R L L C L V L T Y S P A L A
P W L V L T R P P T Y S P A Y L L A R L L G A L V G T Y S P A Y L L A R L L C L V L W Y S P T Y L L A R L L C L
V L T Y S P A Y S V W Y F G A L V G T L F G T Y S V W Y L L C L V L W R L G W L A P W L V L C L V L W Y S P T
Y L L A R L L C L V

3'5' Frame 1
S T K Q S R R A S K S t o p V G E Y Q S T K Q S T N Q G A N Q P R R Q S T K Q S K Y Q T E S t o p V P N R V P T K A
P K Y Q T E S t o p A G E S t o p V S T K Q S R R A S K S t o p V G E Y Q S T K Q S R R A S K S t o p A G E S t o p V P T K A
P R R A S K S t o p A G E S t o p V G G R V S T N Q G A K A G E S t o p V S T K Q S R R A S K S t o p V G E Y Q S T K Q S
K Y Q T E S t o p A G E S t o p V S R R V P K Y Q T E S t o p V P N R V G G R V S K S t o p A S T K V P N R V G G R V S R
R A S K Y Q P R R Q G G R V S K Y Q T E S t o p A G E S t o p V S R R V P K Y Q T E Y Q P R R Q P T K A P K Y Q T E
S t o p V P N R V S T K Q S R R A S K S t o p V G E Y Q S T K Q S T N Q G A N Q P R R Q S T K Q S K Y Q T E S t o p V P
N R V P T K A P K Y Q T E S t o p A G E S t o p V S T K Q S R R A S K S t o p V G E Y Q S T K Q S

3'5' Frame 2
V P N R V G G R V S K S t o p A S T K V P N R V P T K A P T N Q G A K V P N R V S T K Q S K Y Q T E Y Q P R R Q S
T K Q S R R A S K S t o p V P N R V G G R V S K S t o p A S T K V P N R V G G R V S R R A S K Y Q P R R Q G G R V S
R R A S K S t o p A G E S t o p V P T K A P R R A S K S t o p V P N R V G G R V S K S t o p A S T K V P N R V S T K Q S R
R A S K S t o p V G E Y Q S T K Q S K Y Q T E S t o p A G E S t o p V S R R V P K Y Q T E S t o p A G E S t o p V G G R V S T
N Q G A K A G E S t o p V S T K Q S R R A S K S t o p V G E Y Q S T K Q S T N Q G A N Q P R R Q S T K Q S K Y Q T E
S t o p V P N R V G G R V S K S t o p A S T K V P N R V P T K A P T N Q G A K V P N R V S T K Q S K Y Q T E Y Q P R
R Q S T K Q S R R A S K S t o p V P N R V G G R V S K S t o p A S T K V P N R V

3'5' Frame 3
Y Q T E S t o p A G E S t o p V S R R V P K Y Q T E Y Q P R R Q P T K A P K Y Q T E S t o p V P N R V S T K Q S T N Q G
A K V P N R V G G R V S K Y Q T E S t o p A G E S t o p V S R R V P K Y Q T E S t o p A G E S t o p V G G R V S T N Q G A
K A G E S t o p V G G R V S R R A S K Y Q P R R Q G G R V S K Y Q T E S t o p A G E S t o p V S R R V P K Y Q T E S t o p
V P N R V G G R V S K S t o p A S T K V P N R V S T K Q S R R A S K S t o p V G E Y Q S T K Q S R R A S K S t o p A G E
S t o p V P T K A P R R A S K S t o p V P N R V G G R V S K S t o p A S T K V P N R V P T K A P T N Q G A K V P N R V S
T K Q S K Y Q T E S t o p A G E S t o p V S R R V P K Y Q T E Y Q P R R Q P T K A P K Y Q T E S t o p V P N R V S T K Q
S T N Q G A K V P N R V G G R V S K Y Q T E S t o p A G E S t o p V S R R V P K Y Q T E

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Fig.4 Legend. Expasy generated six reading frames from Fig.3 show that there are three ORFs in the 5' 3' direction.

Fig.5

Fig.7

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Query 735 PAAVGAVGGGRRRRKRPVQRGKPPFSYIALIAMATAHSAERRLTLGGIYRFITERFAFYRD 794
          P      GRRRRKRPVQRGKPP+SYIALIAMATA+S ER+LTGGIY+FI ERF FYR+
Sbjct 28 PEEHNQASGGRRRRKRPVQRGKPPSYIALIAMATAANSPEKRLTLGGIYKFIMERFPFYRE 87

Query 795 NPRKWQNSIRHNLTLNDCFVKIPREPGHPGKGNWALDPAAQDMFDSCSFLRRRKRFKRS 854
          N +KWQNSIRHNLTLNDCFVKIPREPGHPGKGNYW LDPAA+DMFD+GSFLRRRKRFKR+
Sbjct 88 NSKKWQNSIRHNLTLNDCFVKIPREPGHPGKGNWTLDPAAEDMFDNGSFLRRRKRFKRT 147

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This domain was re-blastped to NCBI and we found that this domain is highly conserved amongst a number of organisms who are distantly related in evolution [Fig.8].

Fig. 8 Legend. Conserved protein domain obtained from Fig. 7 when blastped into NCBI proteindatabase

This result shows that starting with a sixteen base-pair unique stretch of DNA and using L-System production rule one can make a conserve protein domain which was hitherto unknown to biologists. We predict that this shows all conserved protein domains in living organisms have been produced. This mathematical exercise also clearly shows after a conserved protein domain is formed the biological system does not allow any more conserved domain to be formed from the same sequence by producing a repetitive DNA sequence.

Therefore we can conclude that L-System is an important mathematical tool which can be explored to find out the genomic domain shuffling, protein domain formation and repetitive DNA evolution of different organisms. It is tempting to speculate that natural systems might have used this kind of context free L-System derived methodology to generate genomes of different organisms. This method also could be used by synthetic biologist to find correlation between different organismal DNA, protein domain and finally change them at will.

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