Calculation on Fusion Stability on [DNA or RNA]- Peptide (FS) Algorithm "Cruz-Rodriguez "

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Abstract

During the last few decades, biotechnology has evolved into the construction of chemical chimeras of DNA/RNA fused to segments of proteins named peptides utilizing in this fusion a sequence of amino acids designated as spacing arm. This fusion is done with the goal of complementing or empowering the biological actions of one or both molecules, which, separately, present very low or null biological action, however, due to the fusion a functionally inert molecule could translate into a biochemically active tool. In the present work we present theoretical results of the ideal value of Fusion Stability (FS) at a value of 100%, measured in values of Cruz. For the calculation of FS=[abcd], we have assigned a constant value to one unit, the multiplication value of "bd", where FS= 1[ac]. In the linear equation it represents, the corresponding angle is ¥=45º. We have calculated the values for FS for an amplitude of ¥=45º in a variable range for the size Poly (A), primer size, size Poly Cys and the size of the peptide. We have reached the value FS=100 Cruz for the size 12 nucleotide (nt) of Poly (A), 8 aminoacid (aa) of size Poly Cys, 16 aa of size of the peptide and 24 nt size of primer [DNA or RNA]. We can conclude that the FS value is a predictive value of stability in Silico of a hybrid molecule [DNA or RNA]-peptide where the size of the peptide provides the greatest contribution to the accuracy of the FS value. Values greater than 60 Cruz are indicators in Silico of the chemical stability and biological functionality of a given chimera. This is of great value in the design of vaccines and conjugate medications.*

Keywords: Size Primer [DNA or RNA], Chimera, Size Poly (A), Size Poly Cys, Size Peptide, Fusion Stability (FS), nt, aa, Biological, Geological, Medical Activities.

Introduction

During the last few decades biotechnology has evolved into the construction of chemical chimeras of DNA/RNA fused to segments of proteins named peptides. This fusion is done with the goal of complementing or empowering biological activities of a particular molecule involved in this fusion. The conjugate vaccine has been a pioneer in the application of this fusion tool between nucleic acids and peptides [1].

Biotechnology in the last few decades has evolved into building chimeras from the starting point of sequences [DNA or RNA] of variable sizes in nucleotides (nt) fused to segments of proteins named peptides. In such a fusion in some cases a sequence of amino acids is utilized (aa) named as a spacing arm with Cysteine being the most utilized aa. This fusion is done with the goal of complementing or empowering the biological actions of one or both molecules, which, separately, present a very low or null biological action. However, due to the fusion of functionally inert molecules this could lead to a tridimensional configuration (3D) that provides the new

molecule a biochemically active structure [2].

The design of miRNA-peptide vaccines got their start in the decade of the 80`s when researchers put out their evidence in their publications "Cellular response to respiratory viruses with particular reference to children with disorders of cell-mediated immunity" [3,4].

Also, molecular fusion is utilized between molecules such as: RNA-RNA, cDNA-cDNA, peptide-peptide, cDNA-RNA, cDNA-peptide; it would be a challenge to develop a mathematical algorithm to represent the fusion between molecules such as: RNA-RNA, cDNA-cDNA, peptide-peptide, cDNA-RNA, cDNA-peptide, which would open the doors wide to the biotechnology, biopharmaceutical and cosmetology industries [5].

An emerging discipline, dedicated to the study of the environmental impact on human health, and medical geology is taking the lead in deciphering the enigmas of nature focusing its research on the planet as a priority and of human beings in the aggregate [6,7,8,9,10].

Materials and Methods

In the present work we present the technical result of the calculated value of fusion stability (FS) between primers of miRNA and peptides. We have utilized segments of range primers between 3-45 nt, Poly (A) range between 3-15 nt, Poly Cys range between 3-15 aa and peptides range between 3-45 aa. We have worked on the first stage of performing the calculation of FS assigning the size of the DNA primer at 21 nt, the size of Poly (A) at 6 nt, the size of the Poly Cys at 6 aa (spacing arm between fused molecules) with the objective of calculating the optimum size of the candidate peptide to be fused with the primer (**Figure 1** below).

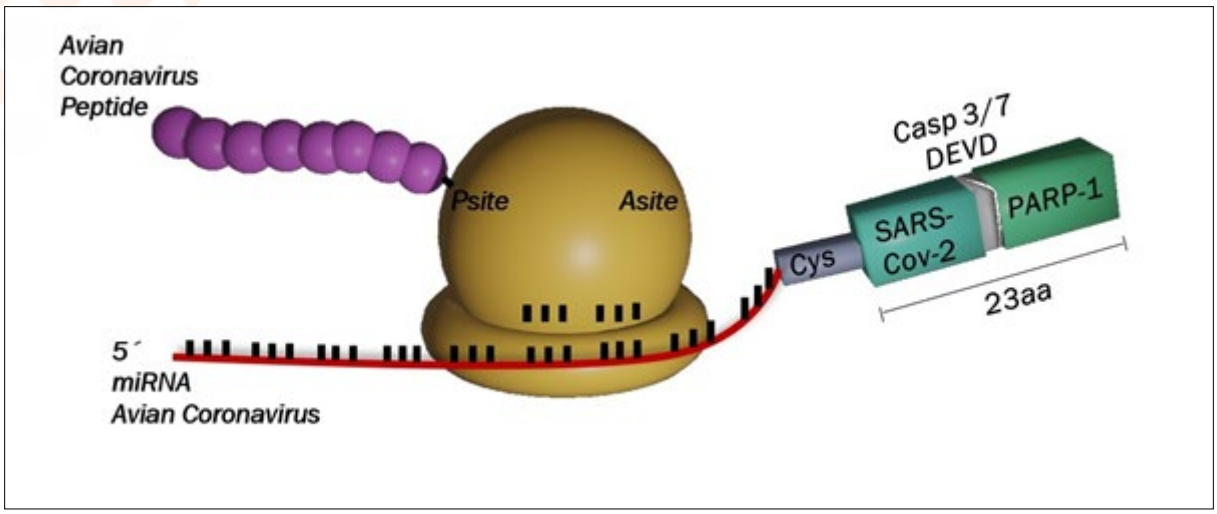

Figure 1 indicates fusion stability (FS) between primers of miRNA and peptide (spacing arm (Poly Cys) and fused molecules SARS-CoV-2 and PARP-1).

The mathematical formula utilized for estimating the stability of the fusion between DNA and the selected peptide is:

FS=abcd, where :

$$a=\frac{S_{PolyA}}{S_{PolyCys}},\quad b=\frac{MW_{miRNA}}{MW_{Peptide}},\quad c=\frac{S_{Peptide}}{S_{miRNA}},\quad d=\frac{[2(A+\beta)+3(C+G)]}{X(pI_1, pI_2, \ldots, pI_n)},$$

S_{PolyA} : *Poly (A) size*

$S_{PolyCys}$: *Poly Cys size*

MW_{miRNA} : *miRNA Molecular Weight*

$MW_{Peptide}$: *Peptide Molecular Weight*

$S_{Peptide}$: *Peptide size [aa]*

S_{miRNA} : *miRNA Size*

ß= T if DNA or ß=U if RNA
pI: point Isoelectric
n: peptide size

This formula has been developed by Dr. Luis CRUZ-RODRIGUEZ and named Fusion Stability Curve (FS): CRUZ-RODRIGUEZ. Its unit of measurement has been named "Cruz". The ideal value for reference of FS is 100 Cruz, such that a result of FS=64.28 Cruz is equivalent to a value of 64.28% with respect to the ideal fusion between a DNA or RNA primer and a peptide, as is the case in the fusion performed for the study of candidate vaccines against covid-19 [11,12].

When the calculated value of FS is greater than 100% then this conjugate fusion would replace the reference value becoming a new combined ideal of reference. For a calculation of FS=[abcd], we have assigned as a constant value for one unit the value of the multiplication of "bd", where FS= 1*[ac]. In the linear equation which it represents the corresponding angle is ¥=45º. We have calculated the values of FS for an amplitude of ¥=45º in a variable range of sizes for the size Poly (A), size range Poly Cys and the size of the peptide.

Results and Discussion

Given the fusion stability formula:

FS= *abcd where :*

$$a = \frac{S_{Poly\,A}}{S_{Poly\,Cys}}, \quad b = \frac{MW_{miRNA}}{MW_{Peptide}}, \quad c = \frac{S_{Peptide}}{S_{miRNA}},$$

$$d = \frac{[2(A+B)+3(C+G)]}{\bar{X}(pI_1, pI_2, \ldots, pI_n)},$$

keeping b and d constant (applying the criteria of "Ceteris paribus", keeping other things constant, to simplify the analysis) and equal to one (bd=1), then:

FS = ac

In this manner, those variables related to size would affect fusion stability (FS):

$$a = \frac{S_{Poly\,A}}{S_{Poly\,Cys}}, \quad c = \frac{S_{Peptide}}{S_{miRNA}},$$

A range of 15 values will be analyzed for each variable and once again the criteria of "Ceteris paribus" will be used to assign values to three of them to then analyze the behavior of the remaining variable in an independent fashion.

To assign the size values in the calculation of **Table 1**(below) the median of the set will be used as the representative figure.

Set	Median
Size Poly Cys (aa)	8
Size peptide (aa)	8
Size DNA or RNA (nt)	24

Table 1 : indicates in each case the value FS=50%, which represents the mean of the fusion stability set.

Size Poly A (nt)	Size Poly Cys (aa)	Size peptide (aa)	Size DNA or RNA (nt)	FS*100 (Cruz)
3	8	8	24	12,5
6	8	8	24	25,0
9	8	8	24	37,5
12	8	8	24	50,0
15	8	8	24	62,5
18	8	8	24	75,0
21	8	8	24	87,5
24	8	8	24	100,0
27	8	8	24	112,5
30	8	8	24	125,0
33	8	8	24	137,5
36	8	8	24	150,0
39	8	8	24	162,5
42	8	8	24	175,0
45	8	8	24	187,5

Table 2: Analysis of FS varying the size of the Poly A.

In **Table 2** the values of Size Poly A are distributed in multiples of 3 due to the frame of reading in codons made up by three nucleotides (from 3 nt to 45 nt). The value 12 nt is highlighted in green color since this value is obtained from the mean FS=50%.

$$FS100 = 100\,\frac{S_{Poly\,A}\,S_{Peptide}}{S_{Poly\,Cys}\,S_{miRNA}}$$

$$FS100 = 100\,\frac{S_{Poly\,A}}{8}\,x\,\frac{8}{24}$$

Size Poly A (nt)	Size Poly Cys (aa)	Size peptide (aa)	Size DNA or RNA (nt)	FS*100 (Cruz)
12	1	8	24	400,00
12	2	8	24	200,00
12	3	8	24	133,33
12	4	8	24	100,00
12	5	8	24	80,00
12	6	8	24	66,67
12	7	8	24	57,14
12	8	8	24	50,00
12	9	8	24	44,44
12	10	8	24	40,00
12	11	8	24	36,36
12	12	8	24	33,33
12	13	8	24	30,77
12	14	8	24	28,57
12	15	8	24	26,67

Table 3: Analysis of FS varying the size of Poly Cys

In Table 3 the values of Size Poly Cys (spacing arm) are distributed in sizes from 1 aa to 15 aa. They are highlighted with the color green for the value 8 aa as this value is obtained from the mean FS=50%.

$$FS100 = 100 \frac{S_{Poly\,A}\, S_{Peptide}}{S_{PolyCys}\, S_{miRNA}}$$

$$FS100 = 100 \frac{12}{S_{PolyCys}} x \frac{8}{24}$$

Size Poly A (nt)	Size Poly Cys (aa)	Size peptide (aa)	Size DNA or RNA (nt)	FS*100 (Cruz)
12	8	1	24	6,25
12	8	2	24	12,50
12	8	3	24	18,75
12	8	4	24	25,00
12	8	5	24	31,25
12	8	6	24	37,50
12	8	7	24	43,75
12	8	8	24	50,00
12	8	9	24	56,25
12	8	10	24	62,50
12	8	11	24	68,75
12	8	12	24	75,00
12	8	13	24	81,25
12	8	14	24	87,50
12	8	15	24	93,75

Table 4 : Analysis of FS varying the size of the peptide.

In Table 4 the values of Size Peptide are distributed in sizes from 1 aa to 15 aa. The value of 8aa is highlighted in green color as this value is obtained from the mean FS=50%.

$$FS100 = 100 \frac{S_{Poly\,A}\, S_{Peptide}}{S_{PolyCys}\, S_{miRNA}}$$

$$FS100 = 100 \frac{12}{8} x \frac{S_{Peptide}}{24}$$

Size Poly A (nt)	Size Poly Cys (aa)	Size peptide (aa)	Size DNA or RNA (nt)	FS*100 (Cruz)
12	8	8	3	400,00
12	8	8	6	200,00
12	8	8	9	133,33
12	8	8	12	100,00
12	8	8	15	80,00
12	8	8	18	66,67
12	8	8	21	57,14
12	8	8	24	50,00
12	8	8	27	44,44
12	8	8	30	40,00
12	8	8	33	36,36
12	8	8	36	33,33
12	8	8	39	30,77
12	8	8	42	28,57
12	8	8	45	26,67

Table 5: Analysis of FS varying the size of the miRNA.
In Table 5 the values of Size DNA or RNA are distributed in multiples of 3 due to the frame of reading in codons made up by three nucleotides (from 3 nt to 45 nt). The value 12 nt is highlighted in green color since this value is obtained from the mean FS=50%.

$$FS100 = 100\frac{S_{Poly\,A}\,S_{Peptide}}{S_{PolyCys}\,S_{miRNA}}$$

$$FS100 = 100\frac{12}{8}\,x\,\frac{8}{S_{miRNA}}$$

Size Poly A (nt)	Size Poly Cys (aa)	Size peptide (aa)	Size DNA or RNA (nt)	FS*100 (Cruz)
12	8	1	24	6,25
12	8	2	24	12,50
12	8	3	24	18,75
12	8	4	24	25,00
12	8	5	24	31,25
12	8	6	24	37,50
12	8	7	24	43,75
12	8	8	24	50,00
12	8	9	24	56,25
12	8	10	24	62,50
12	8	11	24	68,75
12	8	12	24	75,00
12	8	13	24	81,25
12	8	14	24	87,50
12	8	15	24	93,75
12	8	16	24	100,00

Table 6: Stability Function at 100%

Table 6 highlights in yellow color the value FS=100 Cruz for the size of 12 nt of Poly (A), 8 aa size Poly Cys, 16 aa size of peptide and 24 nt size of primer [DNA or RNA].

$$FS100 = 100\frac{S_{Poly\,A}\,S_{Peptide}}{S_{PolyCys}\,S_{miRNA}}$$

$$FS100 = 100\frac{12}{8}\,x\,\frac{16}{24}$$

$$FS100 = 100$$

Conclutions and Perspectives

We can conclude that the FS value is a predictive value of stability in Silico of a hybrid molecule [DNA or RNA]-peptide where the size of the peptide provides the greatest contribution to the accuracy of the FS value. Values greater than 60 Cruz are indicators in Silico of the chemical stability and biological functionality of a given chimera. This is of great value in the design of vaccines and conjugate medications.

For the first time we provide the calculation for fusion stability where it would be a challenge to perform a mathematical algorithm to represent the fusion between molecules such as: RNA-RNA, cDNA-cDNA, peptide-peptide, cDNA-RNA, cDNA-peptide, which would open the doors wide to industries such as: biotechnology, biopharmaceuticals and cosmetology [5, 13].

An emerging discipline, dedicated to the study of the environmental impact on human health, and medical geology is taking the lead in deciphering the enigmas of nature focusing its research on the planet as a priority and of human beings in the aggregate.

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