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Supplementary Information

The Role of the Conformational Dynamics of Glutathione S-Transferase Epsilon Class on Insecticide Resistance in *Anopheles gambiae*

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 Identities = 114/218 (52%), Positives = 166/218 (76%), Gaps = 2/218 (1%)

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Query  125  DIPEDRVEYVQKSYELLEDTLVDDFVAGPTMTIADFSCISTISSIMGVVPLEQSKHPRIY  184
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Sbjct  189  AWIERLSRTLPEYDQLNQEGAVEFAEICESLRLKNGAS  226  AgGCTe5
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Figure S1. Pairwise sequence alignment of the target sequence AgGSTE5 against template sequence AgGSTE2 through the BLAST algorithm.[1] The alignment between target and template sequences displayed a sequence homology with similarity and identity levels of 76 and 52%, respectively.

*e-mail: thereza.soares@ufpe.br

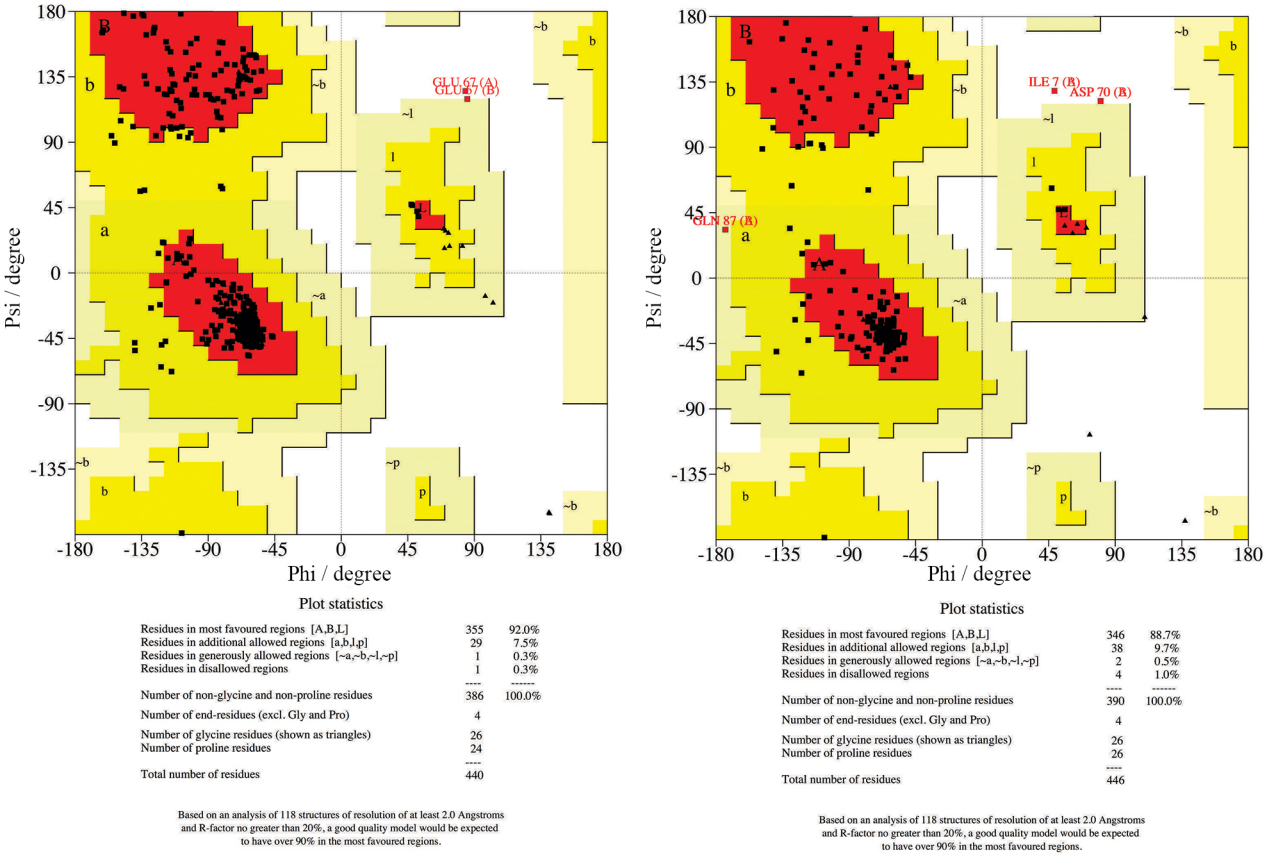
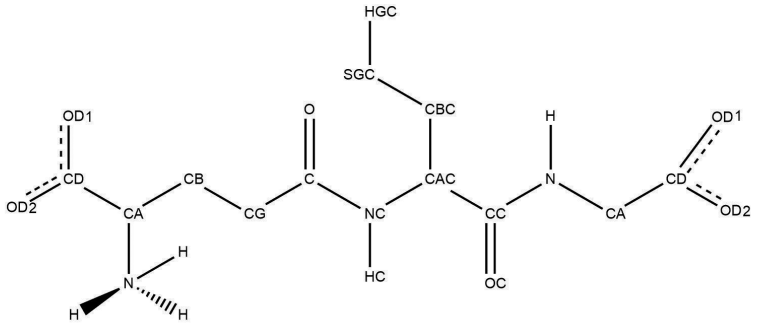


Figure S2. Comparison of Ramachandran plots of (a) the X-ray structure 2IMI solved at 1.4 Å; (b) the structural model of AgGSTE5 in order to assess the stereochemical plausibility of the latter.



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N	NL	0.129	HC	H	0.31
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H2	H	0.248	CBC	CH2	0.15
H3	H	0.248	SGC	S	-0.37
CA	CH1	0.127	HGC	H	0.22
CB	CH2	0	CC	C	0.45
CG	CH2	0	OC	O	-0.45
CD	C	0.27	N	N	-0.31
OD1	OM	-0.635	H	H	0.31
OD2	OM	-0.635	CA	CH2	0
C	C	0.45	C	C	0.27
O	O	-0.45	O1	OM	-0.635
NC	N	-0.31	O2	OM	-0.635

N-H1	gb_2	NC-CAC	gb_21
N-H2	gb_2	CAC-CBC	gb_27
N-H3	gb_2	CAC-CC	gb_27
N-CA	gb_21	CBC-SGC	gb_32
CA-CD	gb_27	SGC-HGC	gb_8
CA-CB	gb_27	CC-OC	gb_5
CB-CG	gb_27	CC-N	gb_10
CG-C	gb_27	N-H	gb_2
CD-OD1	gb_6	N-CA	gb_21
CD-OD2	gb_6	CA-C	gb_27
C-O	gb_5	C-O1	gb_6
C-NC	gb_10	C-O2	gb_6
NC-HC	gb_2		

H1-N-H2	ga_10	CA-CD-OD2	ga_22	CBC-SGC-HGC	ga_3
H1-N-H3	ga_10	OD1-CD-OD2	ga_38	CAC-CC-OC	ga_30
H1-N-CA	ga_11	CG-C-O	ga_30	CAC-CC-N	ga_19
H2-N-H3	ga_10	CG-C-NC	ga_19	OC-CC-N	ga_33
H2-N-CA	ga_11	O-C-NC	ga_33	CC-N-H	ga_32
H3-N-CA	ga_11	C-NC-HC	ga_32	CC-N-CA	ga_31
N-CA-CB	ga_13	C-NC-CAC	ga_31	H-N-CA	ga_18
N-CA-CD	ga_13	HC-NC-CAC	ga_18	N-CA-C	ga_13
CB-CA-CD	ga_13	NC-CAC-CBC	ga_13	CA-C-O1	ga_22
CA-CB-CG	ga_15	NC-CAC-CC	ga_13	CA-C-O2	ga_22
CB-CG-C	ga_13	CBC-CAC-CC	ga_13	O1-C-O2	ga_38
CA-CD-OD1	ga_22	CAC-CBC-SGC	ga_16		

H1-N-CA-CB	gd_14	C-NC-CAC-CBC	gd_39
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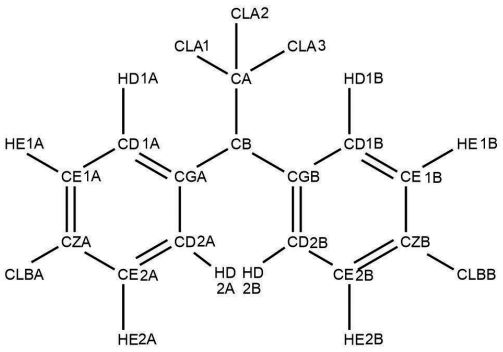
N-CA-CD-OD1	gd_40	CAC-CBC-SGC-HGC	gd_26
CA-CB-CG-C	gd_34	CAC-CC-N-CA	gd_14
CB-CG-C-O	gd_34	CC-N-CA-C	gd_39
CG-C-NC-CAC	gd_14	N-CA-C-O2	gd_40

CA-N-CD-CB	gi_2	CAC-NC-CC-CBC	gi_2
CA-OD2-OD1-CD	gi_1	CC-CAC-N-OC	gi_1
C-CG-NC-O	gi_1	N-C-CA-H	gi_1
NC-C-CAC-HC	gi_1	C-CA-O2-O1	gi_1

Figure S3: Force field parameters for GSH molecule using GROMOS nomenclature for bonded terms. Atom types, atom names and atomic partial charges (left on top); bond parameters (right on top); angle parameters (center); dihedral angles (left on bottom) and improper terms (right on bottom).



Atom Name	Atom Type	Partial Charge (*e*)	Atom Name	Atom Type	Partial Charge (*e*)
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CLA3	CL	0.0407	CGB	C	0.0447
CA	CH0	-0.3479	CD1B	C	-0.1550
CB	CH2	0.1156	HD1B	HC	0.1568
CGA	C	0.0447	CD2B	C	-0.1550
CD1A	C	-0.1550	HD2B	HC	0.1568
HD1A	HC	0.1568	CE1B	C	-0.0861
CD2A	C	-0.1550	HE1B	HC	0.1379
HD2A	HC	0.1568	CE2B	C	-0.0861
CE1A	C	-0.0861	HE2B	HC	0.1379
HE1A	HC	0.1379	CZB	C	0.0157
CE2A	C	-0.0861	CLBB	CL	-0.1125
HE2A	HC	0.1379			

CLA1-CA	gb_40	CE2A-HE2A	gb_3
CLA2-CA	gb_40	CE2A-CZA	gb_16
CLA3-CA	gb_40	CZA-CLBA	gb_40
CA-CB	gb_27	CGB-CD1B	gb_16
CB-CGA	gb_27	CGB-CD2B	gb_16
CB-CGB	gb_27	CD1B-HD1B	gb_3
CGA-CD1A	gb_16	CD1B-CE1B	gb_16
CGA-CD2A	gb_16	CD2B-HD2B	gb_3
CD1A-HD1A	gb_3	CE1B-HE1B	gb_3
CD1A-CE1A	gb_16	CD2B-CE2B	gb_16
CD2A-HD2A	gb_3	CE1B-CZB	gb_16
CD2A-CE2A	gb_16	CE2B-HE2B	gb_3
CE1A-HE1A	gb_3	CE2B-CZB	gb_16
CE1A-CZA	gb_16	CZB-CLBB	gb_40

CLA1-CA-CLA2	ga_13	CGA-CD2A-CE2A	ga_27
CLA1-CA-CLA3	ga_13	HD2A-CD2A-CE2A	ga_25
CLA1-CA-CB	ga_13	CD1A-CE1A-HE1A	ga_25
CLA2-CA-CLA3	ga_13	CD1A-CE1A-CZA	ga_27
CLA2-CA-CB	ga_13	HE1A-CE1A-CZA	ga_25
CLA3-CA-CB	ga_13	CD2A-CE2A-HE2A	ga_25
CA-CB-CGA	ga_15	CD2A-CE2A-CZA	ga_27
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CGA-CB-CGB	ga_15	CE1A-CZA-CE2A	ga_27
CB-CGA-CD1A	ga_27	CE1A-CZA-CLBA	ga_27
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CD1A-CGA-CD2A	ga_27	CB-CGB-CD1B	ga_27
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CGA-CD2A-HD2A	ga_25	CGB-CD1B-HD1B	ga_27

CGB-CD1B-CE1B	ga_25		
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CLA1-CA-CB-CGA	gd_34	CLA3-CA-CB-CGB	gd_34
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CLA2-CA-CB-CGB	gd_34	CA-CB-CGB-CD1B	gd_40
CLA3-CA-CB-CGA	gd_34	CGA-CB-CGB-CD2B	gd_40

CB-CD2A-CD1A-CGA	gi_1	CD2A-CE2A-CZA-CE1A	gi_1	CD1B-CGB-CD2B-CE2B	gi_1
CB-CD2B-CD1B-CGB	gi_1	CD2A-CE2A-CZA-CE1A	gi_1	CD1B-CE1B-CZB-CE2B	gi_1
CGA-CB-CD2A-CD1A	gi_1	CE1A-CD1A-CZA-HE1A	gi_1	CD2B-CGB-CE2B-HD2B	gi_1
CGA-CD1A-CE1A-CZA	gi_1	CE1A-CZA-CD1A-HE1A	gi_1	CD2B-CE2B-CGB-HD2B	gi_1
CGA-CD2A-CE2A-CZA	gi_1	CE1A-CLBA-CE2A-CZA	gi_1	CD2B-CGB-CD1B-CE1B	gi_1
CD1A-CGA-CE1A-HD1A	gi_1	CE2A-CZA-CD2A-HE2A	gi_1	CD2B-CE2B-CZB-CE1B	gi_1
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CD2A-CE2A-CGA-HD2A	gi_1	CD1B-CGB-CE1B-HD1B	gi_1	CE2B-CZB-CD2B-HE2B	gi_1
CD2A-CGA-CD1A-CE1A	gi_1	CD1B-CGB-CE1B-HD1B	gi_1	CZB-CE1B-CE2B-CLBB	gi_1

Figure S4. Force field parameters for DDT molecule using GROMOS nomenclature for bonded terms. Atom types, atom names and atomic partial charges (right on top); bond parameters (left on the middle); angle parameters (right on middle); dihedral angles (left on bottom) and improper terms (right on bottom).

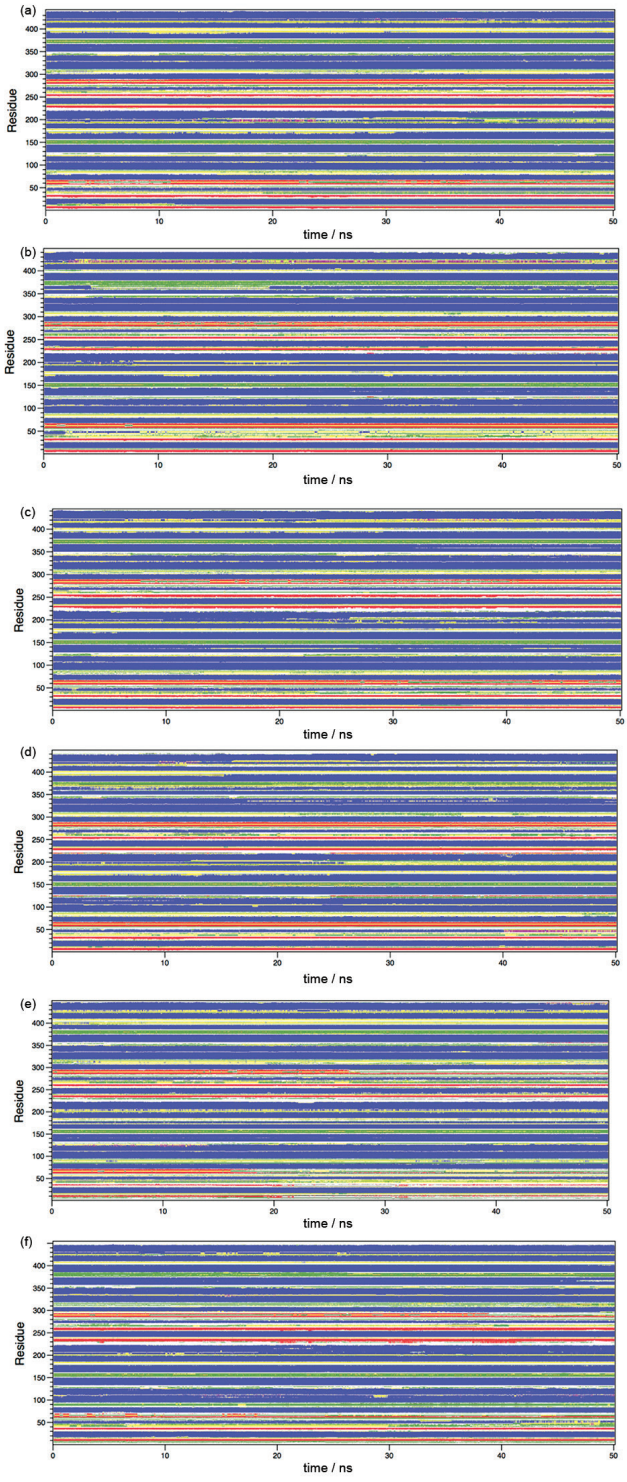

Figure S5. Time-evolution of the secondary structure elements for subunits of the holoform AgGSTE2 (a, b), AgGSTE2-I114T/F120L (c, d) and AgGSTE5 (e, f) during 50 ns of simulation. Secondary structure definition according to Kabsch and Sander.[2] Analyses were carried out over intervals of 5 ps.

References

1. Dunbrack, R. L.; *Curr. Opin. Struct. Biol.* **2006**, *16*, 374.
2. Kabsch, W.; Sander, C.; *Biopolymers* **1993**, *22*, 2577.