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Supporting Material

In silico Phosphorylation of the Autoinhibited Form of $p47^{phox}$: Insights into the Mechanism of Activation

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Table S1: Parameters utilised for the HPO_4^- group

[PSO]				
[atoms]				
N	N	-0.280		0
H	H	0.280		0
CA	CH1	0.000		1
CB	CH2	0.150		2
OP	OA	-0.360		2
P1	P	0.360		2
OM1	OM	-0.635		2
OM2	OM	-0.635		2
OM3	OA	-0.548		2
HP	H	0.398		2
C	C	0.380		3
O	O	-0.380		3
[bonds]				
N	H	gb_2		
N	CA	gb_20		
CA	C	gb_26		
C	O	gb_4		
C	+N	gb_9		
CA	CB	gb_26		
CB	OP	gb_17		
OP	P1	gb_27		
P1	OM1	gb_23		
P1	OM2	gb_23		
P1	OM3	gb_27		
HP	OM3	gb_1		
[angles]				
-C	N	H	ga_31	
H	N	CA	ga_17	
-C	N	CA	ga_30	
N	CA	C	ga_12	
CA	C	+N	ga_18	
CA	C	O	ga_29	
O	C	+N	ga_32	
N	CA	CB	ga_12	
C	CA	CB	ga_12	
CA	CB	OP	ga_8	
CB	OP	P1	ga_25	
OP	P1	OM1	ga_13	
OP	P1	OM2	ga_13	
OP	P1	OM3	ga_13	
P1	OM3	HP	ga_11	
OM1	P1	OM2	ga_28	
OM2	P1	OM3	ga_28	
OM1	P1	OM3	ga_28	
[impropers]				
N	-C	CA	H	gi_1
C	CA	+N	O	gi_1
CA	N	C	CB	gi_2
P	OP	OM1	OM2	gi_2
P	OP	OP	OM1	gi_2
P	OP	OP	OM2	gi_2
[dihedrals]				
-CA	-C	N	CA	gd_4
-C	N	CA	C	gd_19
N	CA	C	+N	gd_20
CA	CB	OP	P1	gd_12
CB	OP	P1	OM2	gd_11
CB	OP	P1	OM1	gd_11
CB	OP	P1	OM3	gd_11
OP	P1	OM3	HP	gd_11

Table S2: Energy decomposition values for the systems studied

		sSH3 (start)	sSH3 (20ns)	sSH3-3P (start)	sSH3-3P (50ns)	sSH3-3P (ED1) (4ns)	sSH3-DP (20ns)
$SH3_A$-$SH3_B$	Coul	-59 (9)	**-36** (8)	-43 (7)	**-205** (18)	**-65** (11)	**-103** (17)
	LJ	-135 (8)	-158 (9)	-133 (9)	-148 (12)	-97 (7)	-154 (9)
$SH3_A$-Polybasic	Coul	-331 (24)	**-344** (20)	-330 (31)	**-517** (31)	**-360** (23)	**-230** (22)
	LJ	-252 (16)	-263 (14)	-236 (13)	-457 (22)	-261 (16)	-248 (13)
$SH3_B$-Polybasic	Coul	-418 (37)	**-306** (22)	-371 (35)	**-302** (30)	**-273** (28)	**-431** (34)
	LJ	-283 (17)	-344 (13)	-295 (18)	-293 (14)	-287 (14)	-363 (18)
$SH3_A$-SOL	Coul	-3973 (126)	**-4184** (113)	-3817 (152)	**-3627** (102)	**-4016** (103)	**-3969** (82)
	LJ	-354 (53)	-306 (48)	-371 (46)	-251 (46)	-371 (45)	-329 (50)
$SH3_B$-SOL	Coul	-4438 (263)	**-4437** (106)	-4222 (153)	**-4141** (133)	**-4473** (116)	**-4506** (102)
	LJ	-225 (52)	-203 (52)	-287 (52)	-243 (48)	-273 (46)	-190 (55)
Polybasic-SOL	Coul	-3248 (124)	**-2734** (118)	-3622 (121)	**-3281** (126)	**-3497** (163)	**-3072** (111)
	LJ	-591 (51)	-511 (48)	-600 (51)	-451 (55)	-637 (53)	-580 (52)

Energies in *(kJ mol^{-1})* fluctuations in parenthesis. Highlighted in bold are the most important changes observed.

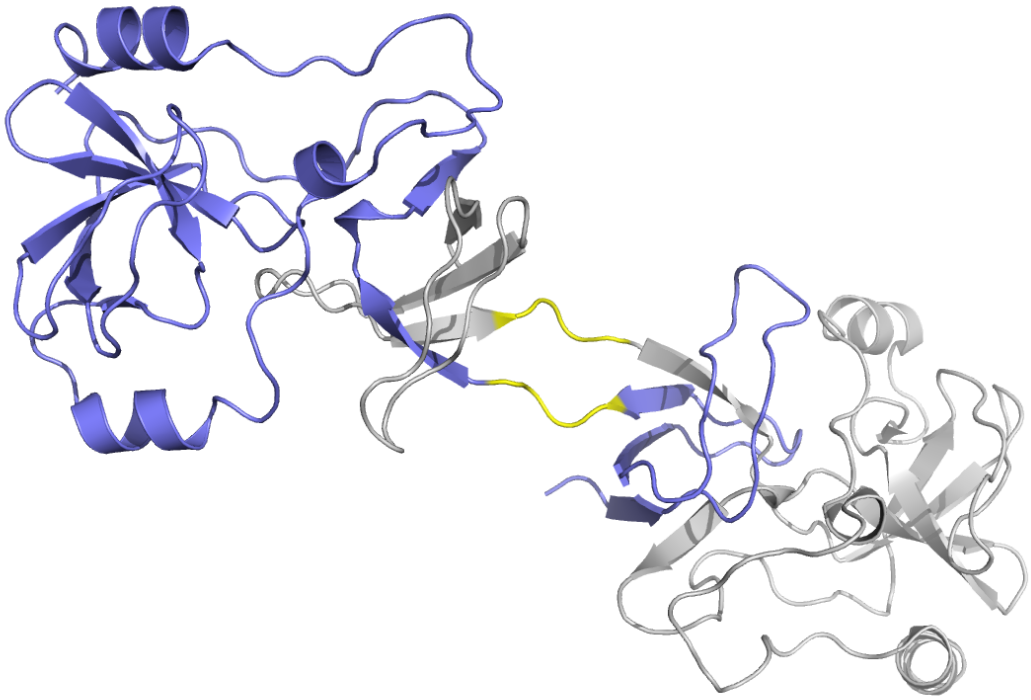

Fig. S1. Structure of p47^{phox} that crystallized as a domain swapped dimer (PDB 1NG2). The domain swapped monomer is shown in blue with the symmetry-related molecule that was used to create the biologically relevant monomer in grey. Residues 198-201 of the distal loop, which where modelled to create the biological monomer are highlighted in yellow.

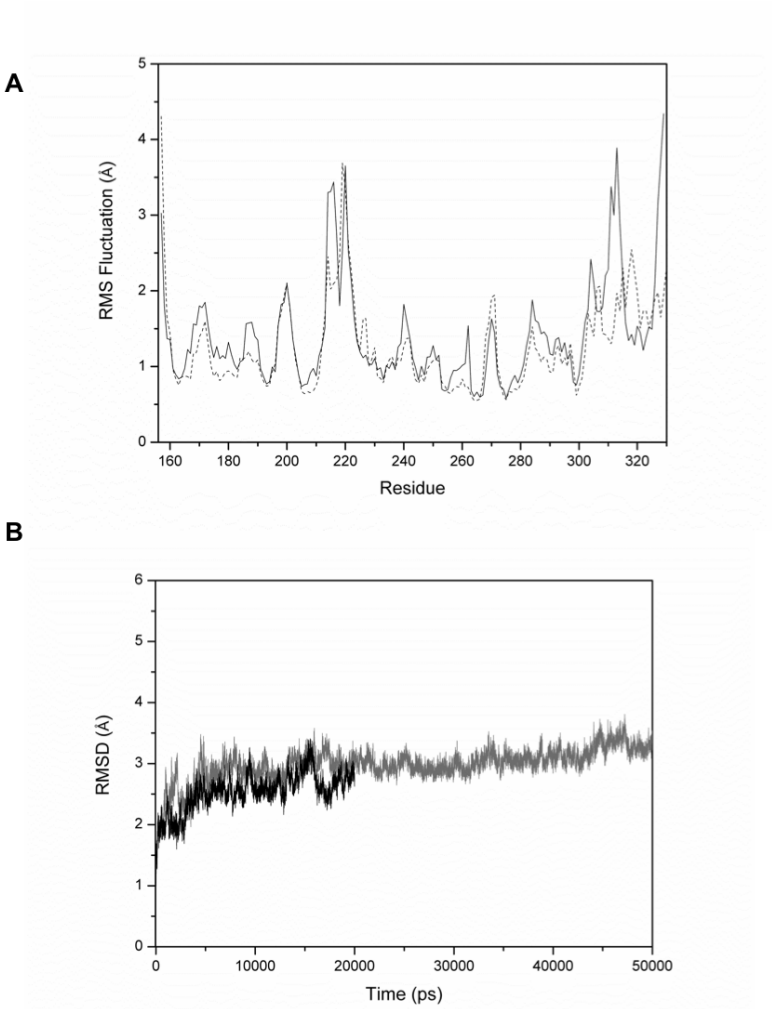

Fig. S2. (*A*) RMSF of the protein backbone with respect to the average position over the entire simulation for sSH3 (*dashed-dotted line*) and for sSH3-3P (*solid line*). (*B*) RMSD of the Cα atoms from their initial coordinates as function of time of sSH3 (*black line*) and sSH3-3P (*gray line*).

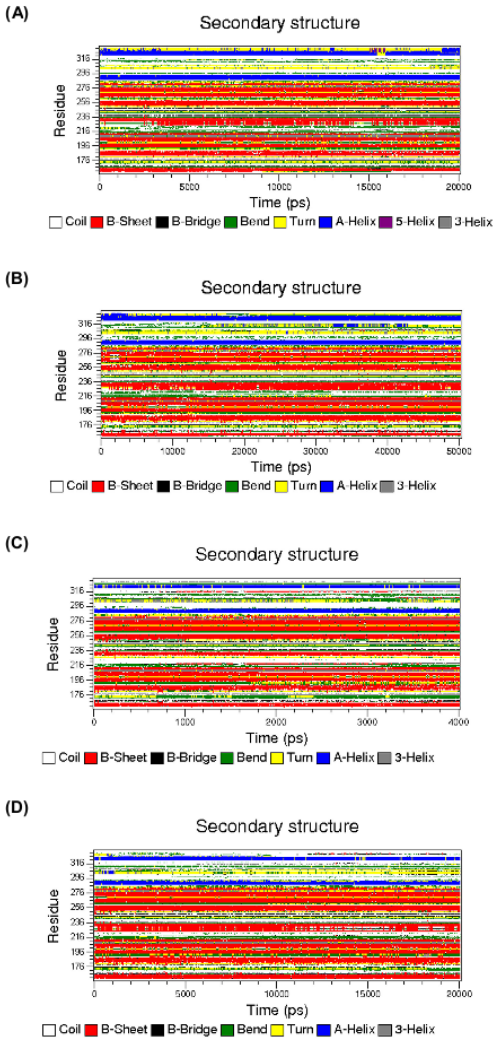

Fig. S3. Time evolution of the secondary structure elements during MD simulations of (*A*) sSH3, (*B*) sSH3-3P, (*C*) ED1ev and (*D*) sSH3-DP. Secondary structure elements at a given time point as determined by DSSP are colored following the scheme:α-helices in blue; β-sheets in red; turns in yellow; bends in green.

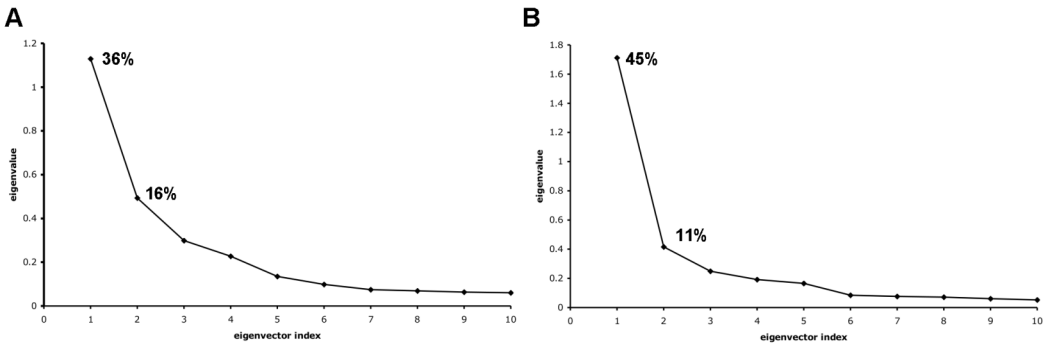

Fig. S4. Eigenvalues as a function of the eigenvector index obtained from essential dynamics analyses for (*A*) sSH3 and (*B*) sSH3-3P. Only the first 10 largest eigenvalues are shown out of a total of 528.

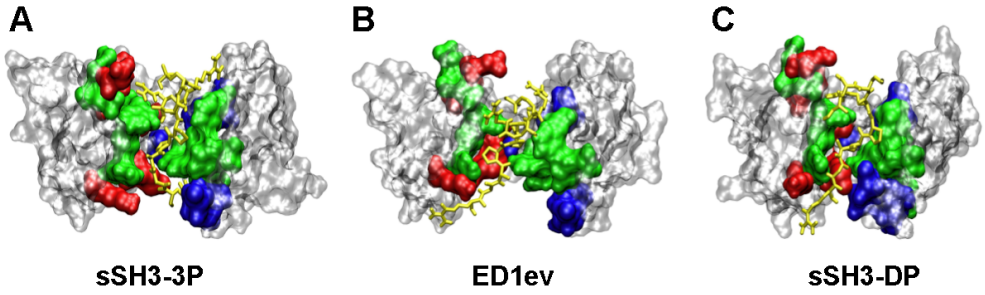

Fig. S5. Surface representation of (*A*) sSH3-3P, (*B*) ED1ev and (*C*) sSH3-DP structures at the end of the corresponding simulated time. The molecular surfaces of the residues in contact with the polybasic region (within 5Å) of $SH3_A$ and $SH3_B$ are displayed in blue and red, respectively. The residues that interact with $p22^{phox}$ are highlighted in green (see Table 2). In licorice (*yellow*) the residues of the PBR/AIR region are shown.

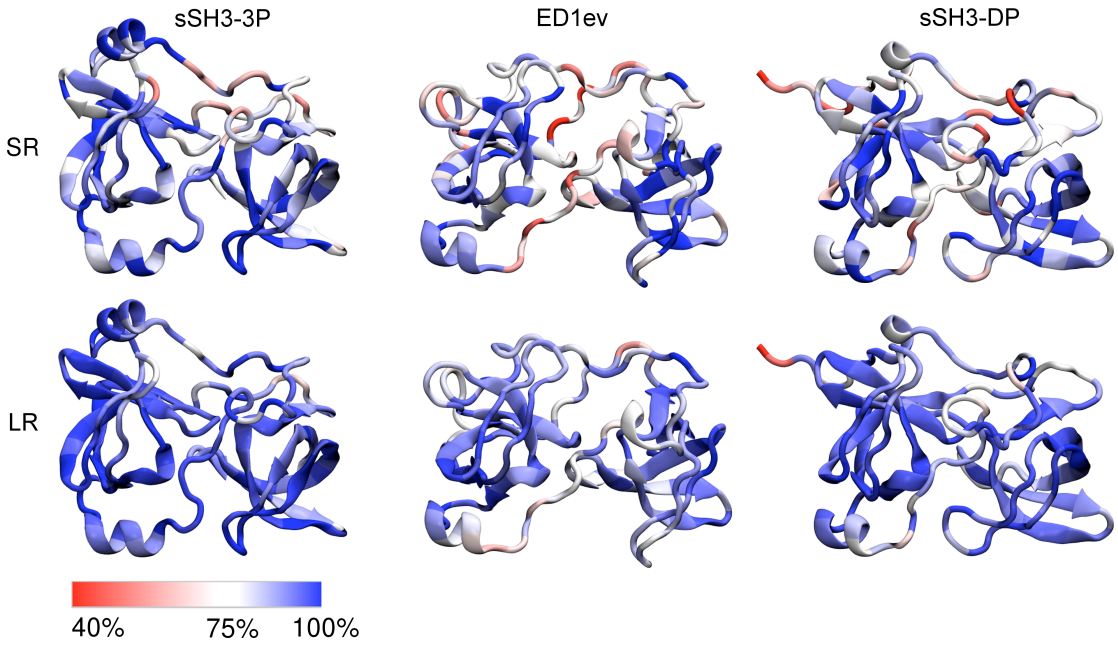

Fig S6. Percentage of conserved native contacts color-mapped onto sSH3-3P (*left*), ED1ev (*middle*) and sSH3-DP (*right*). Short-range (*upper panel*) and long-range (*lower panel*) contacts are reported for each residue using a 6-Å and a 15-Å cutoff, respectively. The distance between residues is calculated as the minimum distance over all the atom pairs. The colour scale ranges from red (low conservation) to blue (high conservation).