

Table S1. Table of Reactions. The model considers a maximum of 20 damage foci and the index *i* identifies species associated with processes relating to individual foci; the addition of *\_2* is added to accommodate modification of species, e.g. DNA-PK sDSB Complex<sub>*i*</sub><sub>*\_2*</sub> represents phosphorylated DNA-PK sDSB Complex.

Reaction ID	Reaction Formulae
<i>rea</i>	Background Sources of Damage -> ROS
<i>rebi</i>	ROS + DNA <sub><i>i</i></sub> -> "Simple DSB" <sub><i>i</i></sub>
<i>rec</i>	ROS -> "ROS Degradation"
<i>redi</i>	uKu70/80 -> Ku70/80 <sub><i>i</i></sub> ; "Simple DSB" <sub><i>i</i></sub>
<i>reei</i>	Ku70/80 <sub><i>i</i></sub> -> uKu70/80
<i>refi</i>	Simple DSB <sub><i>i</i></sub> + Ku70/80 <sub><i>i</i></sub> -> "Ku70/80 sDSB Complex" <sub><i>i</i></sub>
<i>regi</i>	Ku70/80 DSB Complex <sub><i>i</i></sub> -> "Simple DSB" <sub><i>i</i></sub> + Ku70/80 <sub><i>i</i></sub>
<i>rehi</i>	uDNA-PKcs -> "DNA-PKcs" <sub><i>i</i></sub> ; "Simple DSB" <sub><i>i</i></sub>
<i>reii</i>	DNA-PKcs <sub><i>i</i></sub> -> "uDNA-PKcs"
<i>reji</i>	Ku70/80 sDSB Complex <sub><i>i</i></sub> + "DNA-PKcs" <sub><i>i</i></sub> -> "DNA-PK sDSB Complex" <sub><i>i</i></sub>
<i>reDNAPKai</i>	DNA-PK sDSB Complex <sub><i>i</i></sub> -> "Simple DSB" <sub><i>i</i></sub> + Ku70/80 <sub><i>i</i></sub> + "DNA-PKcs" <sub><i>i</i></sub>
<i>reki</i>	DNA-PK sDSB Complex <sub><i>i</i></sub> -> "DNA-PK sDSB Complex" <sub><i>i</i></sub> <sub><i>_2</i></sub>
<i>reDNAPKbi</i>	DNA-PK sDSB Complex <sub><i>i</i></sub> <sub><i>_2</i></sub> -> "Simple DSB" <sub><i>i</i></sub> + Ku70/80 <sub><i>i</i></sub> + "DNA-PKcs" <sub><i>i</i></sub>
<i>reli</i>	uLiIV XRCC4 -> "LiIV XRCC4" <sub><i>i</i></sub> ; "DNA-PK sDSB Complex" <sub><i>i</i></sub> <sub><i>_2</i></sub>
<i>remi</i>	LiIV XRCC4 <sub><i>i</i></sub> -> "uLiIV XRCC4"
<i>reni</i>	DNA-PK sDSB Complex <sub><i>i</i></sub> <sub><i>_2</i></sub> + "LiIV XRCC4" <sub><i>i</i></sub> -> "DNA-PK LiIV XRCC4 sDSB Complex" <sub><i>i</i></sub>
<i>reoi</i>	DNA-PK LiIV XRCC4 sDSB Complex <sub><i>i</i></sub> -> DNA <sub><i>i</i></sub> + Ku70/80 <sub><i>i</i></sub> + "DNA-PKcs" <sub><i>i</i></sub> + "LiIV XRCC4" <sub><i>i</i></sub> + "sDSB Accurate Repair"
<i>repi</i>	ROS + DNA <sub><i>i</i></sub> -> "Complex DSB" <sub><i>i</i></sub>
<i>reqi</i>	uKu70/80 -> Ku70/80 <sub><i>i</i></sub> ; "Complex DSB" <sub><i>i</i></sub>
<i>reri</i>	Complex DSB <sub><i>i</i></sub> + Ku70/80 <sub><i>i</i></sub> -> "Ku70/80 cDSB Complex" <sub><i>i</i></sub>
<i>resi</i>	Ku70/80 cDSB Complex <sub><i>i</i></sub> -> "Complex DSB" <sub><i>i</i></sub> + Ku70/80 <sub><i>i</i></sub>
<i>reti</i>	uDNA-PKcs -> "DNA-PKcs" <sub><i>i</i></sub> ; "Complex DSB" <sub><i>i</i></sub>
<i>reui</i>	Ku70/80 cDSB Complex <sub><i>i</i></sub> + "DNA-PKcs" <sub><i>i</i></sub> -> "DNA-PK cDSB Complex" <sub><i>i</i></sub>
<i>reDNAPKci</i>	DNA-PK cDSB Complex <sub><i>i</i></sub> -> "Complex DSB" <sub><i>i</i></sub> + Ku70/80 <sub><i>i</i></sub> + "DNA-PKcs" <sub><i>i</i></sub>
<i>revi</i>	DNA-PK cDSB Complex <sub><i>i</i></sub> -> "DNA-PK cDSB Complex" <sub><i>i</i></sub> <sub><i>_2</i></sub>
<i>reDNAPKdi</i>	DNA-PK cDSB Complex <sub><i>i</i></sub> <sub><i>_2</i></sub> -> "Complex DSB" <sub><i>i</i></sub> + Ku70/80 <sub><i>i</i></sub> + "DNA-PKcs" <sub><i>i</i></sub>
<i>rewi</i>	uLiIV XRCC4 -> "LiIV XRCC4" <sub><i>i</i></sub> ; "DNA-PK cDSB Complex" <sub><i>i</i></sub> <sub><i>_2</i></sub>
<i>rex<sub>i</sub></i>	DNA-PK cDSB Complex <sub><i>i</i></sub> <sub><i>_2</i></sub> + "LiIV XRCC4" <sub><i>i</i></sub> -> "DNA-PK LiIV XRCC4 cDSB Complex" <sub><i>i</i></sub>
<i>rey<sub>i</sub></i>	DNA-PK LiIV XRCC4 cDSB Complex <sub><i>i</i></sub> -> DNA <sub><i>i</i></sub> + Ku70/80 <sub><i>i</i></sub> + "DNA-PKcs" <sub><i>i</i></sub> + "LiIV XRCC4" <sub><i>i</i></sub> + "cDSB Accurate Repair"
<i>reMRNai</i>	ATM <sub><i>i</i></sub> + MRN <sub><i>i</i></sub> -> "MRN ATM Complex" <sub><i>i</i></sub> ; "Simple DSB" <sub><i>i</i></sub>
<i>reMRNbi</i>	ATM <sub><i>i</i></sub> + MRN <sub><i>i</i></sub> -> "MRN ATM Complex" <sub><i>i</i></sub> ; "Ku70/80 sDSB Complex" <sub><i>i</i></sub>
<i>reMRNci</i>	ATM <sub><i>i</i></sub> + MRN <sub><i>i</i></sub> -> "MRN ATM Complex" <sub><i>i</i></sub> ; "Complex DSB" <sub><i>i</i></sub>
<i>reMRNdi</i>	ATM <sub><i>i</i></sub> + MRN <sub><i>i</i></sub> -> "MRN ATM Complex" <sub><i>i</i></sub> ; "Ku70/80 cDSB Complex" <sub><i>i</i></sub>
<i>rezi</i>	H2AX <sub><i>i</i></sub> -> H2AX <sub><i>i</i></sub> <sub><i>_2</i></sub> ; "MRN ATM Complex" <sub><i>i</i></sub>
<i>reaai</i>	H2AX <sub><i>i</i></sub> -> H2AX <sub><i>i</i></sub> <sub><i>_2</i></sub> ; "DNA-PK sDSB Complex" <sub><i>i</i></sub> <sub><i>_2</i></sub>
<i>reabi</i>	H2AX <sub><i>i</i></sub> -> H2AX <sub><i>i</i></sub> <sub><i>_2</i></sub> ; "DNA-PK cDSB Complex" <sub><i>i</i></sub> <sub><i>_2</i></sub>
<i>reaci</i>	H2AX <sub><i>i</i></sub> <sub><i>_2</i></sub> -> "Damage Focus" <sub><i>i</i></sub>
<i>readi</i>	Damage Focus <sub><i>i</i></sub> -> H2AX <sub><i>i</i></sub>
<i>reaei</i>	Damage Focus <sub><i>i</i></sub> + "MRN ATM Complex" <sub><i>i</i></sub> -> "Complete Damage Focus" <sub><i>i</i></sub>
<i>reafi</i>	Complete Damage Focus <sub><i>i</i></sub> -> H2AX <sub><i>i</i></sub> + ATM <sub><i>i</i></sub> + MRN <sub><i>i</i></sub>

<b>reaqi</b>	uPARP -> PARPi; "Simple DSB"
<b>reari</b>	PARPi -> uPARP
<b>reasi</b>	Simple DSBi + PARPi -> "sDSB PARP Complex"
<b>reati</b>	sDSB PARP Complexi -> "Simple DSB" + PARPi
<b>reaii</b>	uLilii -> Liliii; "sDSB PARP Complex"
<b>reavi</b>	Liliii -> uLilii
<b>reawi</b>	sDSB PARP Complexi + Liliii -> "sDSB PARP-Lilii Complex"
<b>reaxi</b>	sDSB PARP-Lilii Complexi -> DNAi + PARPi + Liliii + "sDSB Accurate Repair (PARP)"
<b>reayi</b>	sDSB PARP-Lilii Complexi -> DNAi + PARPi + Liliii + "Deleterious sDSB Repair"
<b>reMRNgi</b>	ATMi + MRNi -> "MRN ATM Complex"; "sDSB PARP Complex"
<b>reazi</b>	uPARP -> PARPi; "Complex DSB"
<b>rebai</b>	Complex DSBi + PARPi -> "cDSB PARP Complex"
<b>rebbi</b>	cDSB PARP Complexi -> "Complex DSB" + PARPi
<b>rebcii</b>	uLilii -> Liliii; "cDSB PARP Complex"
<b>rebdii</b>	cDSB PARP Complexi + Liliii -> "cDSB PARP-Lilii Complex"
<b>rebeii</b>	cDSB PARP-Lilii Complexi -> DNAi + PARPi + Liliii + "cDSB Accurate Repair (PARP)"
<b>rebfii</b>	cDSB PARP-Lilii Complexi -> DNAi + PARPi + Liliii + "Deleterious cDSB Repair"
<b>reMRNhi</b>	ATMi + MRNi -> "MRN ATM Complex"; "cDSB PARP Complex"
<b>reMRNii</b>	ATMi + MRNi -> "MRN ATM Complex"; "DNA-PK DSB Complex"
<b>reMRNji</b>	ATMi + MRNi -> "MRN ATM Complex"; "DNA-PK DSB Complex <sub>2</sub> "
<b>reMRNki</b>	ATMi + MRNi -> "MRN ATM Complex"; "DNA-PK LiIV XRCC4 DSB Complex"
<b>reMRNli</b>	ATMi + MRNi -> "MRN ATM Complex"; "DNA-PK cDSB Complex"
<b>reMRNmi</b>	ATMi + MRNi -> "MRN ATM Complex"; "DNA-PK cDSB Complex <sub>2</sub> "
<b>reMRNni</b>	ATMi + MRNi -> "MRN ATM Complex"; "DNA-PK LiIV XRCC4 cDSB Complex"
<b>reMRNoi</b>	ATMi + MRNi -> "MRN ATM Complex"; "sDSB PARP-Lilii Complex"
<b>reMRNpi</b>	ATMi + MRNi -> "MRN ATM Complex"; "cDSB PARP-Lilii Complex"

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