Appendix: ZOO Specification of *T-cell* statecharts

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1 Introduction

This is the *on-line* appendix of the paper "Autonomous objects and bottom-up composition in ZOO applied to a case study of biological reactivity".

2 Structural View

Class Definitions.

$$CLASS ::= LigandCl \mid TCRCl \mid PTKCl \mid TcellCl$$

$$\begin{array}{|l} subCl : CLASS \leftrightarrow CLASS \\ abstractCl : \mathbb{P}\ CLASS \\ rootCl : \mathbb{P}\ CLASS \\ \hline subCl = \{\} \\ abstractCl = \{\} \\ rootCl = CLASS \setminus \operatorname{dom} subCl \end{array}$$

$$\begin{array}{|l} \mathbb{O} : CLASS \rightarrow \mathbb{P}_1\ OBJ \\ \mathbb{O}_x : CLASS \rightarrow \mathbb{P}_1\ OBJ \\ \hline \operatorname{disjoint} \mathbb{O}_x \\ \forall\, cl : CLASS \bullet \\ \quad \mathbb{O}\ cl = \mathbb{O}_x\ cl \cup \bigcup(\mathbb{O}_x(\!|\ (subCl^+)^{\sim}(\!|\ \{cl\}\ |\!)\ |\!)) \\ \forall\, cl, cl' : CLASS \mid cl \mapsto cl' \in subCl \bullet \\ \quad \mathbb{O}\ cl \subseteq \mathbb{O}\ cl' \end{array}$$

Events.

$$\begin{aligned} Event ::= {} & evBindLigandAndTCR \mid evFreeLigandAndTCR \mid evPTKActive \\ & \mid evPTKInactive \mid evInhibitPathDecay \mid evPositiveSignal \\ & \mid evInhibitorySignal \mid evPosSigOff \end{aligned}$$

Time and timing delays.

$$TIME == \mathbb{Z}$$

$$\begin{array}{|l} BindingDelay : TIME \\ DissociationDelay : TIME \\ ActivationDelay : TIME \\ InactivationDelay : TIME \\ InhibitPathDecay : TIME \\ PosSigDecay : TIME \end{array}$$

Event timing pre-conditions feedback channel.

$$\begin{aligned} TCEvent == \{ & evBindLigandAndTCR, evFreeLigandAndTCR, evPTKActive, \\ & evPTKInactive, evPosSigOff \} \end{aligned}$$

$$EvPreEval == \mathbb{P}\ TCEvent$$

$$\begin{array}{|l} \text{IsTrueEvPre}\_ : \mathbb{P}(TCEvent \times EvPreEval) \\ \hline \forall\, tev : TCEvent;\ evpreEv : EvPreEval \bullet \\ \quad (\text{IsTrueEvPre}(tev, evpreEv)) \Leftrightarrow tev \in evpreEv \end{array}$$

Global pre-conditions feedback channel.

$GPre ::= LigandFrLfreeToLbound \mid PTKFrActiveToBecomingActive \mid TcellActFrActiveToRestingOrAnergic \mid TcellPSFrOffToOnFull \mid TcellPSFrOnDecayToOnFull$

$GPreEval == \mathbb{P}\ GPre$

$\text{IsTrueGPre}_{\_} : \mathbb{P}(GPre \times GPreEval)$

$\forall\, gp : GPre;\ gpreEv : GPreEval \bullet (\text{IsTrueGPre}(gp, gpreEv)) \Leftrightarrow gp \in gpreEv$

3 Class Ligand

3.1 Intensional View

$LigandST ::= Lfree \mid Lbound$

Ligand

$st : LigandST$
$recTm : TIME$

LigandInit

$LigandInitI$
$Ligand'$

$st' = Lfree$
$recTm' = now?$

LigandInitI

$now? : TIME$

Ligand$_\Delta$*FrFreeToBound*

$\Delta Ligand$
$now? : TIME$
$ev? : Event$
$evpreEval? : EvPreEval$
$gpreEval? : GPreEval$

$(\text{IsTrueEvPre}(ev?, evpreEval?)) \Leftrightarrow ev? = evBindingLigandAndTCR \land now? - recTm \geq bindingDelay \land st = Lfree$
$\text{IsTrueEvPre}(ev?, evpreEval?)$
$\text{IsTrueGPre}(LigandFrLfreeToLbound, gpreEval?) \land st = Lbound$
$st' = Lbound$
$recTm' = now?$

Ligand$_\Delta$*FrBoundToFree*

$\Delta Ligand$
$now? : TIME$
$ev? : Event$
$evpreEval? : EvPreEval$

$(\text{IsTrueEvPre}(ev?, evpreEval?))$
$\land\ ev? = evFreeLigandAndTCR$
$\text{IsTrueEvPre}(ev?, evpreEval?)$
$st' = Lfree$
$recTm' = now?$

$Ligand_\Delta DoSomething == Ligand_\Delta FrFreeToBound \lor Ligand_\Delta FrBoundToFree$

$Ligand_\Xi DoNothing == \neg\, (\text{pre}\ Ligand_\Delta DoSomething) \land \Xi Ligand$

$LigandReact == Ligand_\Delta DoSomething \lor Ligand_\Xi DoNothing$

3.2 Extensional View

$\mathbb{S}Ligand == \mathbb{S}\text{Class}[\ \mathbb{O}\ LigandCl, Ligand][\ sLigand/os, stLigand/oSt\ ]$

$\mathbb{S}LigandInit == [\mathbb{S}Ligand\ ' \mid sLigand' = \varnothing \land stLigand' = \varnothing]$

$\Phi\mathbb{S}LigandN$

$\Delta\ \mathbb{S}Ligand$
$Ligand'$
$oLigand! : \mathbb{O}\ LigandCl$

$oLigand! \in \mathbb{O}_x\ LigandCl \setminus sLigand$
$sLigand' = sLigand \cup \{oLigand!\}$
$stLigand' = stLigand \cup \{(oLigand! \mapsto \theta Ligand')\}$

$\mathbb{S}_{\Delta} LigandNew == \exists\, Ligand' \bullet \Phi\mathbb{S} LigandN \land LigandInit$

$\Phi\mathbb{S} LigandU$

$\Delta\mathbb{S} Ligand$
$\Delta Ligand$
$oLigand? : \mathbb{O}\ LigandCl$

$oLigand? \in sLigand$
$\theta Ligand = stLigand\ oLigand?$
$sLigand' = sLigand$
$stLigand' = stLigand \oplus \{(oLigand? \mapsto \theta Ligand')\}$

$\mathbb{S}_{\Delta} LigandReact == \exists\, \Delta Ligand \bullet \Phi\mathbb{S} LigandU \land LigandReact$

4 Class TCR

4.1 Intensional View

$TCRST ::= Tfree \mid Tbound$

TCR

$st : TCRST$

$TCRInit$

TCR'

$st' = Tfree$

$TCR_{\Delta} FrFreeToBound$

ΔTCR
$ev? : Event$
$evpreEval? : EvPreEval$

$ev? = evBindLigandAndTCR$
$\text{IsTrueEvPre}(ev?, evpreEval?)$
$st = Tfree \land st' = Tbound$

$TCR_{\Delta} FrBoundToFree$

ΔTCR
$ev? : Event$
$evpreEval? : EvPreEval$

$ev? = evFreeLigandAndTCR$
$\text{IsTrueEvPre}(ev?, evpreEval?)$
$st = Tbound \land st' = Tfree$

$TCR_{\Delta} DoSomething == TCR_{\Delta} FrFreeToBound \lor TCR_{\Delta} FrBoundToFree$
$TCR_{\Xi} DoNothing == \neg\, (\text{pre}\ TCR_{\Delta} DoSomething) \land \Xi TCR$
$TCRReact == TCR_{\Delta} DoSomething \lor TCR_{\Xi} DoNothing$

4.2 Extensional View

$\mathbb{S} TCR == \mathbb{S}\text{Class}[\mathbb{O}\ TCRCl, TCR][sTCR/os, stTCR/oSt]$
$\mathbb{S} TCRInit == [\mathbb{S} TCR\ ' \mid sTCR' = \varnothing \land stTCR' = \varnothing]$

$\Phi\mathbb{S} TCRN$

$\Delta\mathbb{S} TCR$
TCR'
$oTCR! : \mathbb{O}\ TCRCl$

$oTCR! \in \mathbb{O}_x\ TCRCl \setminus sTCR$
$sTCR' = sTCR \cup \{oTCR!\}$
$stTCR' = stTCR \cup \{(oTCR! \mapsto \theta TCR')\}$

$\mathbb{S}_\Delta\, TCRNew == \exists\, TCR' \bullet \Phi\mathbb{S}\, TCRN \land TCRInit$

$\Phi\mathbb{S}\, TCRU$

$\Delta\mathbb{S}\, TCR$
$\Delta\, TCR$
$oTCR? : \mathbb{O}\ TCRCl$

$oTCR? \in sTCR$
$\theta TCR = stTCR\ oTCR?$
$sTCR' = sTCR$
$stTCR' = stTCR \oplus \{(oTCR? \mapsto \theta TCR')\}$

$\mathbb{S}_\Delta\, TCRReact == \exists \Delta\, TCR \bullet \Phi\mathbb{S}\, TCRU \land TCRReact$

5 Class PTK

5.1 Intensional View

$PTKST ::= Inactive \mid BecomingActive \mid Active \mid BecomingInactive$

PTK

$st : PTKST$
$recTm : TIME$

$PTKInitI$

$now? : TIME$

$PTKInit$

PTK'
$PTKInitI$

$st' = Inactive \land recTm' = now?$

$PTK_\Delta FrInactiveToBecomingActive$

ΔPTK
$ev? : Event$
$now? : TIME$
$evpreEval? : EvPreEval$

$ev? = evBindLigandAndTCR$
$\text{IsTrueEvPre}(ev?, evpreEval?)$
$st = Inactive \land st' = BecomingActive$
$recTm' = now?$

$PTK_\Delta FrBecomingActiveToInactive$

ΔPTK
$now? : TIME$
$ev? : Event$
$evpreEval? : EvPreEval$

$ev? = evFreeLigandAndTCR$
$\text{IsTrueEvPre}(ev?, evpreEval?)$
$st = BecomingActive \land st' = Inactive$
$recTm' = now?$

$PTK_\Delta FrBecomingActiveToActive$

ΔPTK
$now? : TIME$
$ev? : Event$
$evpreEval? : EvPreEval$

$(\text{IsTrueEvPre}(ev?, evpreEval?))$
$\quad \Leftrightarrow ev? = evPTKActive$
$\quad \land now? - recTm = ActivationDelay$
$\text{IsTrueEvPre}(ev?, evpreEval?)$
$st = BecomingActive \land st' = Active$
$recTm' = now?$

$PTK_\Delta FrActiveToBecomingInactive$

ΔPTK
$ev? : Event$
$now? : TIME$
$evpreEval? : EvPreEval$
$gpreEval? : GPreEval$

$ev? = evFreeLigandAndTCR$
$\text{IsTrueEvPre}(ev?, evpreEval?)$
$\text{IsTrueGPre}(PTKFrActiveToBecomingActive,$
$\quad gpreEval?)$
$st = Active \land st' = BecomingInactive$
$recTm' = now?$

$PTK_\Delta FrBecomingInactiveToActive$

ΔPTK
$ev? : Event$
$now? : TIME$
$evpreEval? : EvPreEval$

$ev? = evPosSigOff$
$\text{IsTrueEvPre}(ev?, evpreEval?)$
$st = BecomingInactive \land st' = Active$
$recTm' = now?$

$PTK_\Delta FrBecomingInactiveToInactive$

ΔPTK
$now? : TIME$
$ev? : Event$
$evpreEval? : EvPreEval$

$(\text{IsTrueEvPre}(ev?, evpreEval?))$
$\quad \Leftrightarrow ev? = evPTKInactive$
$\quad \land now? - recTm = InactivationDelay$
$\text{IsTrueEvPre}(ev?, evpreEval?)$
$st = BecomingInactive \land st' = Inactive$
$recTm' = now?$

$$PTK_\Delta DoSomething == PTK_\Delta FrInactiveToBecomingActive \lor PTK_\Delta FrBecomingActiveToActive \lor PTK_\Delta FrBecomingActiveToInactive \lor PTK_\Delta FrBecomingInactiveToActive \lor PTK_\Delta FrActiveToBecomingInactive \lor PTK_\Delta FrBecomingInactiveToInactive$$

$$PTK_\Xi DoNothing == \neg (\text{pre } PTK_\Delta DoSomething) \land \Xi PTK$$

$$PTKReact == PTK_\Delta DoSomething \lor PTK_\Xi DoNothing$$

5.2 Extensional View

$$\mathbb{S}PTK == \mathbb{S}\text{Class}[\mathbb{O}\ PTKCl, PTK][sPTK/os, stPTK/oSt]$$

$$\mathbb{S}PTKInit == [\mathbb{S}PTK\ ' \mid sPTK' = \varnothing \land stPTK' = \varnothing]$$

$\Phi\mathbb{S}PTKN$

$\Delta\mathbb{S}PTK$
PTK'
$oPTK! : \mathbb{O}\ PTKCl$

$oPTK! \in \mathbb{O}_x\ PTKCl \setminus sPTK$
$sPTK' = sPTK \cup \{oPTK!\}$
$stPTK' = stPTK \cup \{(oPTK! \mapsto \theta PTK')\}$

$$\mathbb{S}_\Delta PTKNew == \exists\, PTK' \bullet \Phi\mathbb{S}PTKN \land PTKInit$$

$\Phi\mathbb{S}PTKU$

$\Delta\mathbb{S}PTK$
ΔPTK
$oPTK? : \mathbb{O}\ PTKCl$

$oPTK? \in sPTK$
$\theta PTK = stPTK\ \ oPTK?$
$sPTK' = sPTK$
$stPTK' = stPTK \oplus \{(oPTK? \mapsto \theta PTK')\}$

$$\mathbb{S}_\Delta PTKReact == \exists \Delta PTK \bullet \Phi\mathbb{S}PTKU \land PTKReact$$

6 Class Tcell

6.1 Intensional View

Component Activation State.

$TcellActStSt ::= Resting \mid StandBy \mid TCActive \mid Anergic$

TcellActSt

$stAct : TcellActStSt$

TcellActStInit

$TcellActSt'$

$stAct' = Resting$

TcellActSt$_\Delta$*FrRestingToStandBy*

$\Delta TcellActSt$
$ev? : Event$
$evpreEval? : EvPreEval$

$ev? = evPTKActive$
$\text{IsTrueEvPre}(ev?, evpreEval?)$
$stAct = Resting$
$stAct' = StandBy$

TcellActSt$_\Delta$*FrStandByToAnergic*

$\Delta TcellActSt$
$ev? : Event$

$ev? = evInhibitorySignal$
$stAct = StandBy$
$stAct' = Anergic$

TcellActSt$_\Delta$*FrStandByToActive*

$\Delta TcellActSt$
$ev? : Event$

$ev? = evPositiveSignal$
$stAct = StandBy$
$stAct' = TCActive$

TcellActSt$_\Delta$*FrActiveToResting*

$\Delta TcellActSt$
$ev? : Event$
$gpreEval? : GPreEval$
$evpreEval? : EvPreEval$

$ev? = evPosSigOff$
$\text{IsTrueEvPre}(ev?, evpreEval?)$
$\text{IsTrueGPre}(TcellActFrActiveToRestingOrAnergic, gpreEval?)$
$stAct = TCActive$
$stAct' = Resting$

TcellActSt$_\Delta$*FrActiveToAnergic*

$\Delta TcellActSt$
$ev? : Event$
$evpreEval? : EvPreEval$
$gpreEval? : GPreEval$

$ev? = evPosSigOff$
$\text{IsTrueEvPre}(ev?, evpreEval?)$
$\neg\ (\text{IsTrueGPre}(TcellActFrActiveToRestingOrAnergic, gpreEval?))$
$stAct = TCActive \land stAct' = Anergic$

$TcellActSt_\Delta DoSomething == TcellActSt_\Delta FrRestingToStandBy$
$\quad \lor\ TcellActSt_\Delta FrStandByToAnergic \lor TcellActSt_\Delta FrStandByToActive$
$\quad \lor\ TcellActSt_\Delta FrActiveToResting \lor TcellActSt_\Delta FrActiveToAnergic$

$TcellActSt_\Xi DoNothing == \neg\ (\text{pre}\ TcellActSt_\Delta DoSomething) \land \Xi TcellActSt$

$TcellActStReact == TcellActSt_\Delta DoSomething \lor TcellActSt_\Xi DoNothing$

Component Inhibitory Pathway.

$TcellIPSt ::= IPOff \mid IPOnFull \mid IPOnDecay$

TcellIP

$stIP : TcellIPSt$
$recTmIP : TIME$

TcellIPInitI

$now? : TIME$

TcellIPInit

$TcellIP'$
$TcellIPInitI$

$stIP' = IPOff$
$recTmIP' = now?$

TcellIP$_\Delta$*FrOffToOnFull*

$\Delta TcellIP$
$ev? : Event$
$now? : TIME$
$evpreEval? : EvPreEval$

$ev? = evPTKActive$
$\text{IsTrueEvPre}(ev?, evpreEval?)$
$stIP = IPOff \land stIP' = IPOnFull$
$recTmIP' = now?$

TcellIP$_\Delta$*FrOnFullToOnDecay*

$\Delta TcellIP$
$ev? : Event$
$now? : TIME$
$evpreEval? : EvPreEval$

$ev? = evPTKInactive$
$\text{IsTrueEvPre}(ev?, evpreEval?)$
$stIP = IPOnFull$
$stIP' = IPOnDecay$
$recTmIP' = now?$

TcellIP$_\Delta$*FrOnDecayToOnFull*

$\Delta TcellIP$
$ev? : Event$
$now? : TIME$
$evpreEval? : EvPreEval$

$ev? = evPTKActive$
$\text{IsTrueEvPre}(ev?, evpreEval?)$
$stIP = IPOnDecay$
$stIP' = IPOnFull$
$recTmIP' = now?$

TcellIP$_\Delta$*FrOnDecayToOff*

$\Delta TcellIP$
$ev? : Event$
$now? : TIME$

$ev? = evInhibitPathDecay$
$now? - recTmIP = InhibitPathDecay$
$stIP = IPOnDecay \land stIP' = IPOff$
$recTmIP' = now?$

$TcellIP_\Delta DoSomething == TcellIP_\Delta FrOffToOnFull$
$\quad \lor TcellIP_\Delta FrOnFullToOnDecay \lor TcellIP_\Delta FrOnDecayToOnFull$
$\quad \lor TcellIP_\Delta FrOnDecayToOff$

$TcellIP_\Xi DoNothing == \neg (\text{pre } TcellIP_\Delta DoSomething) \land \Xi TcellIP$

$TcellIPReact == TcellIP_\Delta DoSomething \lor TcellIP_\Xi DoNothing$

Component Positive Signaling.

$TcellPSSt ::= PSOff \mid PSOnFull \mid PSOnDecay$

TcellPS

$stPS : TcellPSSt$
$recTmPS : TIME$

TcellPSInitI

$now? : TIME$

TcellPSInit

$TcellPS'$
$TcellPSInitI$

$stPS' = PSOff$
$recTmPS' = now?$

TcellPS$_\Delta$*FrOffToOnFull*

$\Delta\, TcellPS$
$ev? : Event$
$now? : TIME$
$gpreEval? : GPreEval$
$evpreEval? : EvPreEval$

$ev? = evPTKActive$
IsTrueEvPre($ev?$, $evpreEval?$)
IsTrueGPre($TcellPSFrOffToOnFull$, $gpreEval?$)
$stPS = PSOff \land stPS' = PSOnFull$
$recTmPS' = now?$

TcellPS$_\Delta$*FrOnFullToOnDecay*

$\Delta\, TcellPS$
$ev? : Event$
$now? : TIME$
$evpreEval? : EvPreEval$

$ev? = evPTKInactive \land$ IsTrueEvPre($ev?$, $evpreEval?$)
$\lor\ ev? = evInhibitorySignal$
$\lor\ ev? = evFreeLigandAndTCR$
$\quad \land$ IsTrueEvPre($ev?$, $evpreEval?$)
$stPS = PSOnFull \land stPS' = PSOnDecay$
$recTmPS' = now?$

TcellPS$_\Delta$*FrOnDecayToOnFull*

$\Delta\, TcellPS$
$ev? : Event$
$now? : TIME$
$evpreEval? : EvPreEval$
$gpreEval? : GPreEval$

$ev? = evPTKActive$
IsTrueEvPre($ev?$, $evpreEval?$)
IsTrueGPre($TcellPSFrOnDecayToOnFull$, $gpreEval?$)
$stPS = PSOnDecay$
$stPS' = PSOnFull$
$recTmPS' = now?$

TcellPS$_\Delta$*FrOnDecayToOff*

$\Delta\, TcellPS$
$ev? : Event$
$now? : TIME$
$evpreEval? : EvPreEval$

(IsTrueEvPre($ev?$, $evpreEval?$))
$\quad \Leftrightarrow ev? = evPosSigOff$
$\quad \land now? - recTmPS = PosSigDecay$
IsTrueEvPre($ev?$, $evpreEval?$)
$stPS = PSOnDecay$
$stPS' = PSOff$
$recTmPS' = now?$

$TcellPS_\Delta DoSomething == TcellPS_\Delta FrOffToOnFull$
$\quad \lor\ TcellPS_\Delta FrOnFullToOnDecay \lor TcellPS_\Delta FrOnDecayToOff$
$TcellPS_\Xi DoNothing == \neg\ (\text{pre}\ TcellPS_\Delta DoSomething) \land \Xi TcellPS$
$TcellPSReact == TcellPS_\Delta DoSomething \lor TcellPS_\Xi DoNothing$

Tcell composition of orthogonal states.

Tcell

$TcellActSt$
$TcellIP$
$TcellPS$

TcellInit

$TcellActStInit$
$TcellIPInit$
$TcellPSInit$

TcellInitI

$TcellIPInitI$
$TcellPSInitI$

$TcellReact == TcellActStReact \land TcellIPReact \land TcellPSReact$

6.2 Extensional View

$\mathbb{S}\, Tcell == \mathbb{S}\text{Class}[\mathbb{O}\ TcellCl, Tcell][sTcell/os, stTcell/oSt]$
$\mathbb{S}\, TcellInit == [\mathbb{S}\, Tcell\ ' \mid sTcell' = \varnothing \land stTcell' = \varnothing]$

$\Phi\mathbb{S}\,TcellN$

$\Delta\mathbb{S}\,Tcell$
$Tcell'$
$oTcell! : \mathbb{O}\ TcellCl$

$oTcell! \in \mathbb{O}_x\ TcellCl \setminus sTcell$
$sTcell' = sTcell \cup \{oTcell!\}$
$stTcell' = stTcell \cup \{(oTcell! \mapsto \theta Tcell')\}$

$\mathbb{S}_\Delta\, TcellNew == \exists\, Tcell' \bullet \Phi\mathbb{S}TcellN \land TcellInit$

$\Phi\mathbb{S}\,TcellU$

$\Delta\mathbb{S}\,Tcell$
$\Delta\,Tcell$
$oTcell? : \mathbb{O}\ TcellCl$

$oTcell? \in sTcell$
$\theta Tcell = stTcell\ \ oTcell?$
$sTcell' = sTcell$
$stTcell' = stTcell \oplus \{(oTcell? \mapsto \theta Tcell')\}$

$\mathbb{S}_\Delta\, TcellReact == \exists\, \Delta Tcell \bullet \Phi\mathbb{S}TcellU \land TcellReact$

7 Relational View

$\mathbb{A}Bind == [rBind : \mathbb{O}LigandCl \leftrightarrow \mathbb{O}TCRCl]$
$\mathbb{A}BindInit == [\mathbb{A}Bind\ ' \mid rBind' = \varnothing]$

$\mathbb{A}\,BindAdd$

$\Delta\mathbb{A}Bind$
$oLigand? : \mathbb{O}LigandCl$
$oTCR? : \mathbb{O}TCRCl$
$ev? : Event$

$ev? = evBindLigandAndTCR$
$rBind' = rBind \cup \{(oLigand? \mapsto oTCR?)\}$

$\mathbb{A}\,BindDel$

$\Delta\mathbb{A}Bind$
$oLigand? : \mathbb{O}LigandCl$
$oTCR? : \mathbb{O}TCRCl$
$ev? : Event$

$ev? = evBindLigandAndTCR$
$rBind' = rBind \setminus \{(oLigand? \mapsto oTCR?)\}$

$\mathbb{A}BindDoSomething == \mathbb{A}BindAdd \lor \mathbb{A}BindDel$
$\mathbb{A}BindDoNothing == \neg\ (\mathrm{pre}\ \mathbb{A}BindDoSomething) \land \Xi\mathbb{A}Bind$
$\mathbb{A}BindReact == \mathbb{A}BindDoSomething \lor \neg\ (\mathrm{pre}\ \mathbb{A}BindDoSomething) \land \Xi\mathbb{A}Bind$

$\mathbb{A}Interact == [rInteract : \mathbb{O}TCRCl \leftrightarrow \mathbb{O}PTKCl]$
$\mathbb{A}InteractInit == [\mathbb{A}Interact\ ' \mid rInteract' = \varnothing]$

$\mathbb{A}\,InteractAdd$

$\Delta\mathbb{A}Interact$
$oTCR? : \mathbb{O}TCRCl$
$oPTK? : \mathbb{O}PTKCl$

$rInteract' = rInteract \cup \{(oTCR? \mapsto oPTK?)\}$

$\mathbb{A}InteractReact == \Xi\mathbb{A}Interact$

$\mathbb{A}ItsTCR == [rItsTCR : \mathbb{O}TcellCl \leftrightarrow \mathbb{O}TCRCl]$
$\mathbb{A}ItsTCRInit == [\mathbb{A}ItsTCR\ ' \mid rItsTCR' = \varnothing]$

$\mathbb{A}ItsTCRAdd$

$\Delta\mathbb{A}ItsTCR$
$oTCR? : \mathbb{O}TCRCl$
$oTcell? : \mathbb{O}TcellCl$

$rItsTCR' = rItsTCR \cup \{(oTcell? \mapsto oTCR?)\}$

$\mathbb{A}ItsTCRReact == \Xi\mathbb{A}ItsTCR$

$\mathbb{A}ItsPTK == [rItsPTK : \mathbb{O}TcellCl \leftrightarrow \mathbb{O}PTKCl]$
$\mathbb{A}ItsPTKInit == [\mathbb{A}ItsPTK\ ' \mid rItsPTK' = \varnothing]$

$\mathbb{A}ItsPTKAdd$

$\Delta\mathbb{A}ItsPTK$
$oPTK? : \mathbb{O}PTKCl$
$oTcell? : \mathbb{O}TcellCl$

$rItsPTK' = rItsPTK \cup \{(oTcell? \mapsto oPTK?)\}$

$\mathbb{A}ItsPTKReact == \Xi\mathbb{A}ItsPTK$

8 Global View

$Link\mathbb{A}Bind$

$\mathbb{S}Ligand$
$\mathbb{S}TCR$
$\mathbb{A}Bind$

$\text{mult}(rBind, sLigand, sTCR, zozo, \{\}, \{\})$

$Link\mathbb{A}Interact$

$\mathbb{S}TCR$
$\mathbb{S}PTK$
$\mathbb{A}Interact$

$\text{mult}(rInteract, sTCR, sPTK, oo, \{\}, \{\})$

$Link\mathbb{A}ItsTCR$

$\mathbb{S}TCR$
$\mathbb{S}Tcell$
$\mathbb{A}ItsTCR$

$\text{mult}(rItsTCR, sTcell, sTCR, oo, \{\}, \{\})$

$Link\mathbb{A}ItsPTK$

$\mathbb{S}PTK$
$\mathbb{S}Tcell$
$\mathbb{A}ItsPTK$

$\text{mult}(rItsPTK, sTcell, sPTK, oo, \{\}, \{\})$

$SysConst == Link\mathbb{A}Bind \land Link\mathbb{A}Interact \land Link\mathbb{A}ItsTCR \land Link\mathbb{A}ItsPTK$

$System$

$\mathbb{S}Ligand;\ \mathbb{S}TCR;\ \mathbb{S}PTK;\ \mathbb{S}Tcell$
$\mathbb{A}Bind;\ \mathbb{A}Interact;\ \mathbb{A}ItsTCR;\ \mathbb{A}ItsPTK$

$SysConst$

$$SysInit == System' \land \mathbb{S}LigandInit \land \mathbb{S}TCRInit \land \mathbb{S}PTKInit \land \mathbb{S}TcellInit \land \mathbb{A}BindInit \land \mathbb{A}InteractInit \land \mathbb{A}ItsTCRInit \land \mathbb{A}ItsPTKInit$$

$$\Psi SysCreateLigand == \Delta System \land \Xi\mathbb{S}Tcell \land \Xi\mathbb{S}TCR \land \Xi\mathbb{S}PTK \land \Xi\mathbb{A}Bind \land \Xi\mathbb{A}Interact \land \Xi\mathbb{A}ItsPTK \land \Xi\mathbb{A}ItsTCR$$

$$SysCreateLigand == \Psi SysCreateLigand \land \mathbb{S}_\Delta LigandNew$$

$$\Psi SysCreateTcell == \Delta System \land \Xi\mathbb{S}Ligand \land \Xi\mathbb{A}Bind$$

$$SysCreateTcell == \Psi SysCreateTcell \land \mathbb{S}_\Delta TcellNew \land \mathbb{S}_\Delta PTKNew \land \mathbb{S}_\Delta TCRNew \land \mathbb{A}ItsTCRAdd[oTCR!/oTCR?, oTcell!/oTcell?] \land \mathbb{A}ItsPTKAdd[oPTK!/oPTK?, oTcell!/oTcell?] \land \mathbb{A}InteractAdd[oPTK!/oPTK?, oTCR!/oTCR?]$$

GPreLigandFrLfreeToLbound

$\mathbb{S}Tcell$
$\mathbb{S}TCR$
$\mathbb{A}ItsTCR$
$oTcell? : \mathbb{O}\ TcellCl$
$gpreEval? : GPreEval$

$\text{IsTrueGPre}(LigandFrLfreeToLbound, gpreEval?)$
$\quad \Leftrightarrow oTcell? \in sTcell \land (stTCR(rItsTCR\ oTcell?)).st = Tfree$

GPrePTKFrActiveToBecomingActive

$\mathbb{S}Tcell$
$\mathbb{S}PTK$
$oTcell? : \mathbb{O}\ TcellCl$
$gpreEval? : GPreEval$

$\text{IsTrueGPre}(PTKFrActiveToBecomingActive, gpreEval?)$
$\quad \Leftrightarrow (stTcell\ oTcell?).stPS = PSOnFull \lor (stTcell\ oTcell?).stPS = PSOnDecay$

GPreTcellActFrActiveToRestingOrAnergic

$\mathbb{A}ItsPTK$
$\mathbb{S}PTK$
$\mathbb{S}Tcell$
$oTcell? : \mathbb{O}\ TcellCl$
$gpreEval? : GPreEval$

$\text{IsTrueGPre}(TcellActFrActiveToRestingOrAnergic, gpreEval?)$
$\quad \Leftrightarrow oTcell? \in sTcell \land (stPTK(rItsPTK\ oTcell?)).st = Inactive$

GPreTcellPSFrOffToOnFull

$\mathbb{A}ItsTCR$
$\mathbb{S}TCR$
$\mathbb{S}Tcell$
$oTcell? : \mathbb{O}\ TcellCl$
$gpreEval? : GPreEval$

$\text{IsTrueGPre}(TcellPSFrOffToOnFull, gpreEval?)$
$\quad \Leftrightarrow oTcell? \in sTcell \land (stTCR(rItsTCR\ oTcell?)).st = Tbound$

GPreTcellPSFrOnDecayToOnFull

$\mathbb{A} ItsTCR$
$\mathbb{S} TCR$
$\mathbb{S} Tcell$
$oTcell? : \mathbb{O}\ TcellCl$
$gpreEval? : GPreEval$

$\text{IsTrueGPre}(TcellPSFrOnDecayToOnFull, gpreEval?)$
$\quad \Leftrightarrow oTcell? \in sTcell \land (stTCR(rItsTCR\ oTcell?)).st = Tbound$

ConnSysReact

$\mathbb{A} ItsTCR;\ \mathbb{A} ItsPTK;\ \mathbb{A} Bind$
$\mathbb{S} TCR;\ \mathbb{S} Tcell;\ \mathbb{S} Ligand$
$oTcell? : \mathbb{O}\ TcellCl$
$oPTK? : \mathbb{O}\ PTKCl$
$oTCR? : \mathbb{O}\ TCRCl$
$oLigand? : \mathbb{O}\ LigandCl$

$oTcell? \in sTcell \land oLigand? \in sLigand$
$oTCR? = rItsTCR\ oTcell? \land oPTK? = rItsPTK\ oTcell?$

$SysObjectsReact == \mathbb{S}_\Delta LigandReact \land \mathbb{S}_\Delta TcellReact \land \mathbb{S}_\Delta PTKReact \land \mathbb{S}_\Delta TCRReact$
$\quad \land \mathbb{A} BindReact \land \mathbb{A} InteractReact \land \mathbb{A} ItsPTKReact \land \mathbb{A} ItsTCRReact \setminus (evpreEval?)$

$SysReactDoSomething == \Delta System \land SysObjectsReact \land ConnSysReact$
$\quad \land GPreLigandFrLfreeToLbound \land GPrePTKFrActiveToBecomingActive$
$\quad \land GPreTcellActFrActiveToRestingOrAnergic \land GPreTcellPSFrOffToOnFull$
$\quad \land GPreTcellPSFrOnDecayToOnFull \setminus (oTCR?, oPTK?, oLigand?, oTcell?, gpreEval?)$

$SysReactDoNothing == \neg (\text{pre}\ SysReactDoSomething) \land \Xi System$

$SysReact == SysReactDoSomething \lor SysReactDoNothing$

A ZOO Toolkit

$[OBJ]$

$\mathbb{S}\text{Class}\ [OS, OST]$

$os : \mathbb{P}\ OS$
$oSt : OS \pfun OST$

$\text{dom}\ oSt = os$

$MultTy ::= mm \mid mo \mid om \mid mzo \mid zom \mid oo \mid zozo \mid zoo \mid ozo \mid ms \mid sm \mid ss$
$\quad \mid so \mid os \mid szo \mid zos$

$[X, Y]$

$\text{mult}\_ : \mathbb{P}((X \leftrightarrow Y) \times \mathbb{P}\, X \times \mathbb{P}\, Y \times \mathit{MultTy} \times \mathbb{F}\, \mathbb{N} \times \mathbb{F}\, \mathbb{N})$

$\forall\, r : X \leftrightarrow Y;\ sx : \mathbb{P}\, X;\ sy : \mathbb{P}\, Y;\ s_1, s_2 : \mathbb{F}\, \mathbb{N} \bullet$
$(\text{mult}(r, sx, sy, mm, s_1, s_2)) \Leftrightarrow r \in sx \leftrightarrow sy$

$\forall\, r : X \leftrightarrow Y;\ sx : \mathbb{P}\, X;\ sy : \mathbb{P}\, Y;\ s_1, s_2 : \mathbb{F}\, \mathbb{N} \bullet$
$(\text{mult}(r, sx, sy, mo, s_1, s_2)) \Leftrightarrow r \in sx \to sy$

$\forall\, r : X \leftrightarrow Y;\ sx : \mathbb{P}\, X;\ sy : \mathbb{P}\, Y;\ s_1, s_2 : \mathbb{F}\, \mathbb{N} \bullet$
$(\text{mult}(r, sx, sy, om, s_1, s_2)) \Leftrightarrow r^\sim \in sy \to sx$

$\forall\, r : X \leftrightarrow Y;\ sx : \mathbb{P}\, X;\ sy : \mathbb{P}\, Y;\ s_1, s_2 : \mathbb{F}\, \mathbb{N} \bullet$
$(\text{mult}(r, sx, sy, mzo, s_1, s_2)) \Leftrightarrow r \in sx \pfun sy$

$\forall\, r : X \leftrightarrow Y;\ sx : \mathbb{P}\, X;\ sy : \mathbb{P}\, Y;\ s_1, s_2 : \mathbb{F}\, \mathbb{N} \bullet$
$(\text{mult}(r, sx, sy, zom, s_1, s_2)) \Leftrightarrow r^\sim \in sy \pfun sx$

$\forall\, r : X \leftrightarrow Y;\ sx : \mathbb{P}\, X;\ sy : \mathbb{P}\, Y;\ s_1, s_2 : \mathbb{F}\, \mathbb{N} \bullet$
$(\text{mult}(r, sx, sy, oo, s_1, s_2)) \Leftrightarrow r \in sx \rightarrowtail sy$

$\forall\, r : X \leftrightarrow Y;\ sx : \mathbb{P}\, X;\ sy : \mathbb{P}\, Y;\ s_1, s_2 : \mathbb{F}\, \mathbb{N} \bullet$
$(\text{mult}(r, sx, sy, zozo, s_1, s_2)) \Leftrightarrow r \in sx \pfun sy$

$\forall\, r : X \leftrightarrow Y;\ sx : \mathbb{P}\, X;\ sy : \mathbb{P}\, Y;\ s_1, s_2 : \mathbb{F}\, \mathbb{N} \bullet$
$(\text{mult}(r, sx, sy, zoo, s_1, s_2)) \Leftrightarrow r \in sx \rightarrowtail sy$

$\forall\, r : X \leftrightarrow Y;\ sx : \mathbb{P}\, X;\ sy : \mathbb{P}\, Y;\ s_1, s_2 : \mathbb{F}\, \mathbb{N} \bullet$
$(\text{mult}(r, sx, sy, ozo, s_1, s_2)) \Leftrightarrow r^\sim \in sy \rightarrowtail sx$

$\forall\, r : X \leftrightarrow Y;\ sx : \mathbb{P}\, X;\ sy : \mathbb{P}\, Y;\ s_1, s_2 : \mathbb{F}\, \mathbb{N} \bullet$
$(\text{mult}(r, sx, sy, ms, s_1, s_2)) \Leftrightarrow (\text{mult}(r, sx, sy, mm, s_1, s_2))$
$\land\ (\forall\, x : \text{dom}\, r \bullet \#(\{x\} \lhd r) \in s_1)$

$\forall\, r : X \leftrightarrow Y;\ sx : \mathbb{P}\, X;\ sy : \mathbb{P}\, Y;\ s_1, s_2 : \mathbb{F}\, \mathbb{N} \bullet$
$(\text{mult}(r, sx, sy, sm, s_1, s_2)) \Leftrightarrow (\text{mult}(r, sx, sy, mm, s_1, s_2))$
$\land\ (\forall\, y : \text{ran}\, r \bullet \#(r \rhd \{y\}) \in s_1)$

$\forall\, r : X \leftrightarrow Y;\ sx : \mathbb{P}\, X;\ sy : \mathbb{P}\, Y;\ s_1, s_2 : \mathbb{F}\, \mathbb{N} \bullet$
$(\text{mult}(r, sx, sy, ss, s_1, s_2)) \Leftrightarrow (\text{mult}(r, sx, sy, ms, s_1, \{\}))$
$\land\ (\text{mult}(r, sx, sy, sm, s_2, \{\}))$

$\forall\, r : X \leftrightarrow Y;\ sx : \mathbb{P}\, X;\ sy : \mathbb{P}\, Y;\ s_1, s_2 : \mathbb{F}\, \mathbb{N} \bullet$
$(\text{mult}(r, sx, sy, so, s_1, s_2)) \Leftrightarrow (\text{mult}(r, sx, sy, mo, s_1, s_2))$
$\land\ (\text{mult}(r, sx, sy, sm, s_1, s_2))$

$\forall\, r : X \leftrightarrow Y;\ sx : \mathbb{P}\, X;\ sy : \mathbb{P}\, Y;\ s_1, s_2 : \mathbb{F}\, \mathbb{N} \bullet$
$(\text{mult}(r, sx, sy, os, s_1, s_2)) \Leftrightarrow (\text{mult}(r, sx, sy, om, \{\}, \{\}))$
$\land\ (\text{mult}(r, sx, sy, ms, s_1, \{\}))$

$\forall\, r : X \leftrightarrow Y;\ sx : \mathbb{P}\, X;\ sy : \mathbb{P}\, Y;\ s_1, s_2 : \mathbb{F}\, \mathbb{N} \bullet$
$(\text{mult}(r, sx, sy, szo, s_1, s_2)) \Leftrightarrow (\text{mult}(r, sx, sy, mzo, \{\}, \{\}))$
$\land\ (\text{mult}(r, sx, sy, sm, s_1, \{\}))$

$\forall\, r : X \leftrightarrow Y;\ sx : \mathbb{P}\, X;\ sy : \mathbb{P}\, Y;\ s_1, s_2 : \mathbb{F}\, \mathbb{N} \bullet$
$(\text{mult}(r, sx, sy, zos, s_1, s_2)) \Leftrightarrow (\text{mult}(r, sx, sy, zom, \{\}, \{\}))$
$\land\ (\text{mult}(r, sx, sy, ms, s_1, \{\}))$