Ion Channels

Table-1: Parameter values for ion-channel dynamics of SNc cell model (Francis et al., 2013).

Constant	Symbol	Value	Units
Faraday's constant	F	96485	$coulomb * mole^{-1}$
SNc membrane capacitance	C_{snc}	$9\ x\ 10^7$	$pF * cm^{-2}$
Cytosolic volume	v_{cyt}	$\phi_{cyt} * v_{pmu}$	pl
Fraction of cytosolic volume	ϕ_{cyt}	0.5	$dimensionless$
Pacemaking unit (PMU) volume	v_{pmu}	5	pl
PMU area	$\mathcal{A}_{pmu}$	$\mathcal{S}_{pmu} * v_{pmu}$	cm^2
PMU surface area-to-volume ratio	$\mathcal{S}_{pmu}$	$1.6667\ x\ 10^4$	cm^{-1}
Voltage defined thermodynamic entity	V_D	$\frac{V}{V_\tau}$	$dimensionless$
Temperature defined thermodynamic entity	V_τ	$\frac{R * T}{F}$	mV
Universal gas constant	R	8314.472	$mJ * mol^{-1} * K^{-1}$
Physiological temperature	T	310.15	K
Maximal conductance of calcium channel	$\bar{g}_{Ca,L}$	2101.2	$pA * mM^{-1}$
Extracellular calcium concentration	$[Ca_e]$	1.8	mM
Reversal potential for calcium ion	V_{Ca}	$\frac{1}{2} * \log\left(\frac{[Ca_e]}{[Ca_i]}\right)$	$dimensionless$
Valence of calcium ion	z_{Ca}	2	$dimensionless$
Maximal conductance of sodium channel	$\bar{g}_{Na}$	907.68	$pA * mM^{-1}$
Extracellular sodium concentration	$[Na_e]$	137	mM
Reversal potential for sodium ion	V_{Na}	$\log\left(\frac{[Na_e]}{[Na_i]}\right)$	$dimensionless$
Valence of sodium ion	z_{Na}	1	$dimensionless$

Maximal conductance of sodium HCN channel	$\bar{g}_{NaHCN}$	51.1	$pA * mM^{-1}$
Maximal conductance of leaky sodium channel	$\bar{g}_{Nalk}$	0.0053	$pA * mM^{-1}$
Cyclic adenosine monophosphate concentration	$[cAMP]$	$1\ x\ 10^{-5}$	mM
Maximal conductance of delayed rectifying potassium channel	$\bar{g}_{Kdr}$	31.237	nS
Extracellular potassium concentration	$[K_e]$	5.4	mM
Reversal potential for potassium ion	V_K	$\log\left(\frac{[K_e]}{[K_i]}\right)$	$dimensionless$
Valence of potassium ion	z_K	1	$dimensionless$
Maximal conductance of inward rectifying potassium channel	$\bar{g}_{Kir}$	13.816	nS
Maximal conductance of small conductance potassium channel	$\bar{g}_{Ksk}$	2.2515	$pA * mM^{-1}$
Maximal conductance for sodium-potassium ATPase	K_{nak}	1085.7	pA
Reaction rates of I_{NaK}	$k_{2,nak}$	0.04	ms^{-1}
	$k_{3,nak}$	0.01	ms^{-1}
	$k_{4,nak}$	0.165	ms^{-1}
Dissociation constants of I_{NaK}	$K_{nak,nae}$	69.8	mM
	$K_{nak,nai}$	4.05	mM
	$K_{nak,ke}$	0.258	mM
	$K_{nak,ki}$	32.88	mM
Maximal conductance for calcium ATPase	k_{pmca}	2.233	$pA * ms^{-1}$
Reaction rates of I_{pmca}	$k_{2,pc}$	0.001	ms^{-1}
	$k_{3,pc}$	0.001	ms^{-1}
	$k_{4,pc}$	1	ms^{-1}
Dissociation constants of I_{pmca}	$K_{pc,e}$	2	mM

Maximal conductance for sodium-calcium exchanger	k_{xm}	0.0166	$pA * ms^{-1}$
Energy barrier parameter of I_{NaCaX}	δ_{xm}	0.35	$dimensionless$
Denominator factor of I_{NaCaX}	$\mathcal{D}_{xm}$	0.001	$dimensionless$

Table-2: Steady state values of ion-channel dynamics of SNc cell model (Francis et al., 2013).

Symbol	Value	Symbol	Value
V	$-49.42\ mV$	h_{Na}	0.1848
$[Ca_i]$	$1.88\ x\ 10^{-4}\ mM$	O_{NaHCN}	0.003
$[Na_i]$	$4.69\ mM$	$m_{K,dr}$	0.003
$[K_i]$	$126.06\ mM$	y_{nak}	0.6213
m_{Na}	0.0952	y_{pc}	0.483

Calcium Buffering Mechanisms

Table-3: Parameter values of calcium buffering mechanisms of SNc cell model (Francis et al., 2013; Marhl et al., 2000).

Constant	Symbol	Value	Units
Calbindin reaction rates	$k_{1,calb}$	10	$mM^{-1} * ms^{-1}$
	$k_{2,calb}$	$2\ x\ 10^{-3}$	ms^{-1}
Total cytosolic calbindin concentration	$[Calb_{tot}]$	0.005	mM
Calmodulin reaction rates	k_{cam}^{cb}	12000	$mM^{-2} * ms^{-1}$
	k_{cam}^{nb}	$3.7\ x\ 10^{6}$	$mM^{-2} * ms^{-1}$
	k_{cam}^{cd}	$3\ x\ 10^{-3}$	ms^{-1}
	k_{cam}^{nd}	3	ms^{-1}
Total cytosolic calmodulin concentration	$[Cam_{tot}]$	0.0235	mM

The maximal rate constant of SERCA	$k_{serca,er}$	0.02	$mM^{-1} * ms^{-1}$
Maximal permeability of calcium channels in the ER membrane	$k_{ch,er}$	3	ms^{-1}
Half saturation for calcium	$K_{ch,er}$	0.005	mM
Maximal rate constant for calcium leak flux through the ER membrane	$k_{leak,er}$	$5 \ x \ 10^{-5}$	ms^{-1}
Ratio of free calcium to total calcium concentration in ER	β_{er}	0.0025	$dimensionless$
Volume ratio between the ER and cytosol	ρ_{er}	0.01	$dimensionless$
Maximal permeability of MCUs	$k_{mcu,mt}$	$3 \ x \ 10^{-4}$	$mM * ms^{-1}$
Half saturation for calcium	$K_{mcu,mt}$	$8 \ x \ 10^{-4}$	mM
Maximal rate of calcium flux through $[Na^{+}]/[Ca^{2+}]$ exchangers and mPTPs	$k_{out,mt}$	0.125	ms^{-1}
Half saturation for calcium	$K_{out,mt}$	0.005	mM
Maximal rate constant for calcium leak flux through the MT membrane	$k_{leak,mt}$	$6.25 \ x \ 10^{-6}$	ms^{-1}
Ratio of free calcium to total calcium concentration in MT	β_{mt}	0.0025	$dimensionless$
Volume ratio between the MT and cytosol	ρ_{mt}	0.01	$dimensionless$

Table-4: Steady state values of calcium buffering mechanisms of SNc cell model (Francis et al., 2013; Marhl et al., 2000).

Symbol	Value	Symbol	Value
$[Ca_{er}]$	$1 \ x \ 10^{-3} \ mM$	$[Calb]$	$26 \ x \ 10^{-4} \ mM$
$[Ca_{mt}]$	$4 \ x \ 10^{-4} \ mM$	$[Cam]$	$222 \ x \ 10^{-4} \ mM$

Energy Metabolism

Table-5: Parameter values of energy metabolism of SNc cell model (Cloutier and Wellstead, 2010, 2012).

Constant	Symbol	Value	Units
Extracellular glucose concentration	$[GLC_e]$	1	mM
Hexokinase maximal flux	$\bar{v}_{hk}$	$2.5\ x\ 10^{-3}$	$mM * ms^{-1}$
Affinity constant for ATP	$K_{m,ATP,hk}$	0.5	mM
Inhibition constant for F6P	$K_{i,F6P}$	0.068	mM
Phosphofructokinase maximal flux	$\bar{v}_{pfk}$	$3.8\ x\ 10^{-3}$	$mM * ms^{-1}$
Affinity constant for F6P	$K_{m,F6P,pfk}$	0.18	mM
Affinity constant for ATP	$K_{m,ATP,pfk}$	0.05	mM
Affinity constant for F26P	$K_{m,F26P,pfk}$	0.01	mM
Activation constant for AMP	$K_{a,AMP,pfk}$	0.05	mM
Inhibition constant for ATP	$K_{i,ATP}$	1	mM
Coefficient constant for AMP	$nAMP$	0.5	$dimensionless$
Coefficient constant for ATP	$nATP$	0.4	$dimensionless$
Total energy shuttles concentration	$[ANP]$	2.51	mM
Coefficient constant for ADP	Q_{adk}	0.92	$dimensionless$
Phosphofructokinase-2 maximal forward flux	$\bar{v}_{pfk2,f}$	$2\ x\ 10^{-7}$	$mM * ms^{-1}$
Phosphofructokinase-2 maximal reverse flux	$\bar{v}_{pfk2,r}$	$1.036\ x\ 10^{-7}$	$mM * ms^{-1}$
Affinity constant for F6P	$K_{m,F6P,pfk2}$	0.01	mM
Affinity constant for ATP	$K_{m,ATP,pfk2}$	0.05	mM
Affinity constant for F26P	$K_{m,F26P,pfk2}$	0.0001	mM
Activation constant for AMP	$K_{a,AMP,pfk2}$	0.005	mM
Pyruvate kinase maximal flux	$\bar{v}_{pk}$	$5\ x\ 10^{-3}$	$mM * ms^{-1}$
Affinity constant for GAP	$K_{m,GAP,pk}$	0.4	mM
Affinity constant for ADP	$K_{m,ADP,pk}$	0.005	mM

Oxidative phosphorylation maximal flux	$\bar{v}_{op}$	$1\ x\ 10^{-3}$	$mM * ms^{-1}$
Maximal electron transport chain efficiency	$\bar{\eta}_{op}$	0.995	$dimensionless$
Maximal fraction of $asyn^{*}$ effect on the oxidative phosphorylation	$\beta_{op,asyn_{mis}}$	0.08	$dimensionless$
Affinity constant for $asyn^{*}$	$K_{asyn_{mis}}$	$8.5\ x\ 10^{-3}$	mM
Affinity constant for PYR	$K_{m,PYR,op}$	0.5	mM
Affinity constant for ADP	$K_{m,ADP,op}$	0.005	mM
Forward reaction constant of LDH	$k_{ldh,f}$	$12.5\ x\ 10^{-3}$	ms^{-1}
Reverse reaction constant of LDH	$k_{ldh,r}$	$2.5355\ x\ 10^{-3}$	ms^{-1}
Maximal lactate fermentation efficiency	$\bar{\eta}_{ldh}$	1	$dimensionless$
Maximal fraction of ROS effect on the lactate fermentation	$\beta_{ldh,ROS}$	0.25	$dimensionless$
Affinity constant for ROS	$K_{ldh,ROS}$	$10\ x\ 10^{-3}$	mM
MCT maximal influx	$\bar{v}_{lac}$	$3.55\ x\ 10^{-4}$	$mM * ms^{-1}$
Coefficient constant for MCT influx	$K_{lac,inf}$	0.641	$dimensionless$
Reaction constant for lactate efflux	$K_{lac,eff}$	$7.1\ x\ 10^{-4}$	ms^{-1}
ATPase maximal flux	$\bar{v}_{ATPase}$	$9.355\ x\ 10^{-4}$	$mM * ms^{-1}$
Affinity constant for ATP	$K_{m,ATP}$	0.5	mM
PPP maximal flux	$\bar{v}_{ppp}$	$3.972\ x\ 10^{-4}$	$mM * ms^{-1}$
Inhibition constant for $\left(\frac{NADPH}{NADP}\right)$	$K_{i,NADPH}$	20	$dimensionless$
Total NADPH and NADP concentration	$[NADPH_{tot}]$	0.25	mM
GR forward reaction constant	$k_{gr,f}$	$1.8\ x\ 10^{-4}$	$mM^{-1} * ms^{-1}$
GR reverse reaction constant	$k_{gr,r}$	$3.472\ x\ 10^{-7}$	$mM^{-1} * ms^{-1}$
Total GSH and GSSG concentration	$[GSH_{tot}]$	2.5	mM
Reaction constant of DOX	$K_{dox,ROS}$	$7.5\ x\ 10^{-8}$	ms^{-1}

CK forward reaction constant	$k_{ck,f}$	$3\ x\ 10^{-3}$	$mM^{-1} * ms^{-1}$
CK reverse reaction constant	$k_{ck,r}$	$1.26\ x\ 10^{-3}$	$mM^{-1} * ms^{-1}$
Total PCr and Cr concentration	$[PCr_{tot}]$	20	mM

Table-6: Steady state values of energy metabolism of SNc cell model (Cloutier and Wellstead, 2010, 2012).

Symbol	Value	Symbol	Value
$[F6P]$	$0.176\ mM$	$[LAC]$	$0.598\ mM$
$[F26P]$	$2.2\ x\ 10^{-3}\ mM$	$[PCr]$	$18.04\ mM$
$[GAP]$	$8.25\ x\ 10^{-2}\ mM$	$[NADPH]$	$0.25\ mM$
$[PYR]$	$0.124\ mM$	$[GSH]$	$2.5\ mM$
$[ATP_i]$	$2.4\ mM$		

Dopamine Turnover Processes

Table-7: Parameter values for DA turnover processes of SNc cell model (Reed et al., 2012; Tello-Bravo, 2012).

Constant	Symbol	Value	Units
Average release flux per vesicle	ψ	17.4391793	$mM * ms^{-1}$
Initial vesicular DA concentration	DA_{v_o}	500	mM
Sensitivity to vesicular DA concentration	DA_{v_s}	0.01	mM
Affinity constant of DA binding to receptors	DA_{R_a}	$5\ x\ 10^{-5}$	mM
Binding sensitivity	DA_{R_s}	0.01	mM
Activation constant for ATP	$K_{a,RRP}$	1.4286	mM
Vesicle recycling maximal flux	$\bar{v}_{nrrp}$	$1\ x\ 10^{-3}$	$mM * ms^{-1}$
Maximal vesicle recycling efficiency	$\bar{\eta}_{nrrp}$	0.995	$dimensionless$
Maximal fraction of $asyn^*$ effect on the vesicle	$\beta_{nrrp,asyn_{mis}}$	0.08	$dimensionless$

Affinity constant for $asyn^*$	$K_{asyn_{mis}}$	$8.5\ x\ 10^{-3}$	mM
Reaction constant of DA_e clearance	k_{comt}	0.0083511	ms^{-1}
Tyrosine concentration	$[TYR]$	$126\ x\ 10^{-3}$	mM
Affinity constant for TYR	K_{TYR}	$46\ x\ 10^{-3}$	mM
Inhibition constant for DA_c	$K_{i,cda}$	$11\ x\ 10^{-2}$	mM
Inhibition constant for DA_e	$K_{i,eda}$	$46\ x\ 10^{-3}$	mM
Maximal velocity of DA synthesis	$\bar{V}_{synt}$	$25\ x\ 10^{-6}$	$mM * ms^{-1}$
Affinity constant for Ca_i	K_{synt}	$35\ x\ 10^{-4}$	mM
Maximal velocity of VMAT	$\bar{V}_{cda}$	$4.67\ x\ 10^{-6}$	ms^{-1}
Affinity constant for DA_c	K_{cda}	$238\ x\ 10^{-4}$	mM
Scaling factor for VMAT	α_{vmat}	$1\ x\ 10^{-3}$	$dimensionless$
Scaling factor for ATP_i	β_{vmat}	3	$dimensionless$
Reaction constant of DA_c clearance	k_{mao}	0.00016	ms^{-1}
Maximal velocity of AADC	$\bar{V}_{aadc}$	$9.73\ x\ 10^{-5}$	$mM * ms^{-1}$
Affinity constant for $LDOPA$	K_{aadc}	0.13	mM
Maximal velocity of AAT	$\bar{V}_{aat}$	$5.11\ x\ 10^{-7}$	$mM * ms^{-1}$
Affinity constant for $LDOPA_e$	K_{ldopa_e}	$3.2\ x\ 10^{-4}$	mM
Affinity constant for TYR_e	K_{tyr_e}	$6.4\ x\ 10^{-4}$	mM
Affinity constant for TRP_e	K_{trp_e}	$1.5\ x\ 10^{-4}$	mM
Serum concentration of TYR	$[TYR_e]$	$6.3\ x\ 10^{-4}$	mM
Serum concentration of TRP	$[TRP_e]$	$8.2\ x\ 10^{-4}$	mM
Serum concentration of LDOPA	$[sLD]$	$3.6\ x\ 10^{-3}$	mM

Table-8: Steady state values of DA turnover processes of SNc cell model (Reed et al., 2012; Tello-Bravo, 2012).

Symbol	Value	Symbol	Value
$[DA_e]$	$4\ x\ 10^{-6}\ mM$	$[DA_v]$	$500\ mM$
$[DA_c]$	$1\ x\ 10^{-4}\ mM$	$[LDOPA]$	$3.6\ x\ 10^{-4}\ mM$

Molecular Pathways Involved in PD Pathology

Table-9: Parameter values of PD pathology pathways of SNc cell model (Cloutier and Wellstead, 2012).

Constant	Symbol	Value	Units
Activation constant for ATP	$K_{a,leak}$	0.5282	mM
Reaction constant for ROS production due to excess dopamine	k_{dopa}	$4.167\ x\ 10^{-4}$	$mM^{-1} * ms^{-1}$
Affinity constant for $[DA_c]$	K_{dopa}	8.5	mM
Reaction constant for catalase	k_{cat}	$2.35\ x\ 10^{-5}$	ms^{-1}
Reaction constant for alpha-synuclein oxidation	k_{syn}	$1.39\ x\ 10^{-8}$	$mM * ms^{-1}$
Reaction constant for alpha-synuclein consumption	k_{to}	$1.39\ x\ 10^{-7}$	ms^{-1}
Reaction constant for alpha-synuclein aggregation	k_{agg}	$2.08\ x\ 10^{-10}$	ms^{-1}
Affinity constant for $ASYN_{mis}$	K_{agg}	$7.5\ x\ 10^{-3}$	mM
Reaction constant for tagging of damaged protein	k_{tag}	$7.64\ x\ 10^{-11}$	$mM^{-1} * ms^{-1}$
Total ubiquitin concentration	$[Ub_{tot}]$	$10.5\ x\ 10^{-3}$	mM
Reaction constant for damaged protein disposal by the proteasome	k_{prt}	$2.08\ x\ 10^{-10}$	ms^{-1}
Affinity constant for $ASYN_{agg}$	K_{prt}	$5\ x\ 10^{-3}$	mM
Fraction reduction of proteasome activity by $ASYN_{agg}$	β_{prt}	0.25	$dimensionless$
Reaction constant for $ASYN_{agg}$ disposal by lysosome	k_{lyso}	$2.08\ x\ 10^{-11}$	ms^{-1}
Reaction constant for Lewy bodies from $ASYN_{agg}$	k_{lb}	$2.08\ x\ 10^{-11}$	ms^{-1}
Affinity constant for $ASYN_{agg}$	K_{lb}	$5\ x\ 10^{-3}$	mM

Table-10: Steady state values of PD pathology pathways of SNc cell model (Cloutier and Wellstead, 2012).

Symbol	Value	Symbol	Value
$[ROS]$	$1\ x\ 10^{-3}\ mM$	$[ASYN_{tag}]$	$1\ x\ 10^{-5}\ mM$
$[ASYN]$	$0.1\ mM$	$[ASYN_{agg}]$	$0\ mM$
$[ASYN_{mis}]$	$1\ x\ 10^{-3}\ mM$	$[LB]$	$0\ mM$

Apoptotic Pathways

Table-11: Parameter values of apoptotic pathways of SNc cell model (Hong et al., 2012).

Constant	Symbol	Value	Units
Forward reaction constant for $[Ca_i.Calpain]$	k_1^+	1	$mM^{-1} * ms^{-1}$
Reverse reaction constant for $[Ca_i.Calpain]$	k_1^-	$1\ x\ 10^{-3}$	ms^{-1}
Forward reaction constant for $[Calpain^*]$	k_2^+	$1\ x\ 10^{-3}$	ms^{-1}
Forward reaction constant for $[Calpain^*.Casp12]$	k_3^+	1	$mM^{-1} * ms^{-1}$
Reverse reaction constant for $[Calpain^*.Casp12]$	k_3^-	$1\ x\ 10^{-3}$	ms^{-1}
Forward reaction constant for $[Casp12^*]$	k_4^+	$1\ x\ 10^{-3}$	ms^{-1}
Forward reaction constant for $[Casp12^*.Casp9]$	k_5^+	10	$mM^{-1} * ms^{-1}$
Reverse reaction constant for $[Casp12^*.Casp9]$	k_5^-	$5\ x\ 10^{-4}$	ms^{-1}
Forward reaction constant for $[Casp9^*]$	k_6^+	$1\ x\ 10^{-3}$	ms^{-1}
Forward reaction constant for $[Casp9^*.Casp3]$	k_7^+	10	$mM^{-1} * ms^{-1}$
Reverse reaction constant for $[Casp9^*.Casp3]$	k_7^-	$5\ x\ 10^{-4}$	ms^{-1}
Forward reaction constant for $[Casp3^*]$	k_8^+	$1\ x\ 10^{-4}$	ms^{-1}
Forward reaction constant for $[Apop]$	k_9^+	1	$mM^{-1} * ms^{-1}$
Forward reaction constant for $[Casp9^*]$	k_{10}^+	$1\ x\ 10^{-3}$	ms^{-1}
Forward reaction constant for $[Casp9^*.IAP]$	k_{11}^+	5	$mM^{-1} * ms^{-1}$
Reverse reaction constant for $[Casp9^*.IAP]$	k_{11}^-	$35\ x\ 10^{-7}$	ms^{-1}
Forward reaction constant for $[Casp3^*.IAP]$	k_{12}^+	5	$mM^{-1} * ms^{-1}$
Reverse reaction constant for $[Casp3^*.IAP]$	k_{12}^-	$35\ x\ 10^{-7}$	ms^{-1}
Forward reaction constant for $[ROS_{mit}]$	k_{13}^+	0.5	$mM^{-1} * ms^{-1}$
Forward reaction constant for $[PTP_{mit}^*]$	k_{14}^+	0.5	$mM^{-1} * ms^{-1}$
Forward reaction constant for $[Cytc]$	k_{15}^+	1	$mM^{-1} * ms^{-1}$
Forward reaction constant for $[Cytc.Casp9]$	k_{16}^+	1	$mM^{-1} * ms^{-1}$
Reverse reaction constant for $[Cytc.Casp9]$	k_{16}^-	$1\ x\ 10^{-3}$	ms^{-1}

Table-12: Steady state values of energy metabolism of SNc cell model (Hong et al., 2012).

Symbol	Value	Symbol	Value
$[Calpain]$	1	$[ROS_{mit}]$	0
$[Ca_i.Calpain]$	0	$[PTP^*_{mit}]$	1
$[Calpain^*]$	0	$[Cytc_{mit}]$	1
$[Casp12]$	1	$[Cytc]$	0
$[Calpain^*.Casp12]$	0	$[Cytc.Casp9]$	0
$[Casp12^*]$	0	$[Casp9]$	1
$[Casp12^*.Casp9]$	0	$[Casp9^*]$	0
$[Casp3]$	1	$[Casp9^*.Casp3]$	0
$[Casp3^*]$	0	$[IAP]$	1
$[Casp9^*.IAP]$	0	$[Casp3^*.IAP]$	0
$[Apop]$	0		

Energy Consumption

Table-13: Parameters for energy consumption processes of SNc cell model.

Constant	Symbol	Value	Units
Faraday's constant	F	96485	$coulomb * mole^{-1}$
Cytosolic volume	v_{cyt}	$\phi_{cyt} * v_{pmu}$	pl
Pacemaking unit (PMU) volume	v_{pmu}	5	pl
Fraction of cytosolic volume	ϕ_{cyt}	0.5	$dimensionless$
Scaling factor for synaptic recycling	λ_{sr}	100	$dimensionless$
Scaling factor for neurotransmitter packing	λ_{np}	1	$dimensionless$
Ratio of free calcium to total calcium concentration in ER	β_{er}	0.0025	$dimensionless$
Volume ratio between the ER and cytosol	ρ_{er}	0.01	$dimensionless$
Scaling factor for proteasome	λ_{prt}	25	$dimensionless$

Scaling factor for ubiquitination	λ_{tag}	3	$dimensionless$
Scaling factor for lysosome	λ_{lyso}	10	$dimensionless$

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