**Moonlighting Proteins -**

**An Approach to Systematize the Concept**

**Supplemental Material**

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This supplement contains the models used to simulate the moonlighting types. Each model can be executed by copying the corresponding code into a Stimator template (<https://webpages.ciencias.ulisboa.pt/~aeferreira/stimator/>) in python. The models contain the reactions and the rates used for the simulations.

# Type IA

#reactions

vin1 : -> A , rate = k1

v2 : A -> B , rate = k2\*A

v3 : B + M -> BM , rate = k3\*B\*M\*(1-External)

v4 : BM -> B + M , rate = k4\*BM

v5 : BM -> C + M , rate = k5\*BM

vin6 : -> X , rate = k6

v7 : X -> Y , rate = k7\*X

v8 : Y + M -> YM , rate = k8\*Y\*M\*External

v9 : YM -> Y + M , rate = k9\*YM

v10: YM -> Z + M , rate = k10\*YM

v11: External -> External , rate = k11

vout12: Z -> , rate = k12\*Z

vout13: C -> , rate = k13\*C

#rates

k1 = 1

k2 = 1

k3 = 1

k4 = 0.1

k5 = 1

k6 = 1

k7 = 1

k8 = 1

k9 = 0.1

k10= 1

k11= 0

k12= 1

k13= 1

#initial conditions

init: (M = 1, External = 0)

#init: (A= 0.9999546006630569, C= 0.7225587222504776, B= 3.217639289972702, YM= 0.0, BM= 0.74172242580507, M= 0.2582775741949304, Y= 9.00004539933694, X= 0.9999546006630569, Z= 0.0)

# Type I B

#reactions

vin1 : -> A , rate = k1

v2 : A -> B , rate = k2\*A

v3 : B + M -> BM , rate = k3\*B\*M

v4 : BM -> B + M , rate = k4\*BM

v5 : BM -> C + M , rate = k5\*BM

vin6 : -> X , rate = k6

v7 : X -> Y , rate = k7\*X

v8 : Y + M -> YM , rate = k8\*Y\*M

v9 : YM -> Y + M , rate = k9\*YM

v10: YM -> Z + M , rate = k10\*YM

v11: B + A -> AB , rate = k11\*A\*B\*step(t, 100, 1)

vout12: Z -> , rate = k12\*Z

vout13: C -> , rate = k13\*C

vout14: AB -> , rate = k14\*AB

#rates

k1 = 1

k2 = 1

k3 = 5

k4 = 0.1

k5 = 1

k6 = 1

k7 = 1

k8 = 1

k9 = 0.1

k10= 1

k11= 0.1

k12 = 1

k13 = 1

k14 = 1

#initial conditions

init: (M=1.0)

# Type I C

#reactions

vin1 : -> A , rate = k1

v2 : A -> B , rate = k2\*A

v3 : B + M -> BM , rate = k3\*B\*M

v4 : BM -> B + M , rate = k4\*BM

v5 : BM -> C + M , rate = k5\*BM

vin6 : -> X , rate = k6

v7 : X -> Y , rate = k7\*X

v8 : Y + M -> YM , rate = k8\*Y\*M\*(1+50\*YM\*step(t, 100, 1))

v9 : YM -> Y + M , rate = k9\*YM

v10: YM -> Z + M , rate = k10\*YM

vout12: Z -> , rate = k12\*Z

vout13: C -> , rate = k13\*C

#rates

k1 = 1

k2 = 1

k3 = 2

k4 = 0.1

k5 = 1

k6 = 1

k7 = 1

k8 = 1

k9 = 0.1

k10= 1

k12 = 1

k13 = 1

#initial conditions

init: (M=1.0)

# Type I D

#reactions

vin1 : -> A , rate = k1

v2 : A -> B , rate = k2\*A

v3 : B + M -> BM , rate = k3\*B\*M

v4 : BM -> B + M , rate = k4\*BM

v5 : BM -> C + M , rate = k5\*BM

vin6 : -> X , rate = k6\*step(t, 100, 1)

v7 : X -> Y , rate = k7\*X

v8 : Y + M -> YM , rate = k8\*Y\*M

v9 : YM -> Y + M , rate = k9\*YM

v10: YM -> Z + M , rate = k10\*YM

vout12: Z -> , rate = k12\*Z

vout13: C -> , rate = k13\*C

#rates

k1 = 1

k2 = 1

k3 = 1

k4 = 0.1

k5 = 1

k6 = 1

k7 = 1

k8 = 1

k9 = 0.1

k10= 1

k11= 0

k12= 1

k13= 1

#initial conditions

init: (M=1.0)

#Typ II A

#reactions

vin1 : -> A , rate = k1

v2 : A -> B , rate = k2\*A

v3 : B + M -> BM , rate = k3\*B\*M\*(1-External)

v4 : BM -> B + M , rate = k4\*BM

v5 : BM -> C + M , rate = k5\*BM

vin6 : -> X , rate = k6

v7 : X -> Y , rate = k7\*X

v8 : Y + M -> YM , rate = k8\*Y\*M\*External

v9 : YM -> Y + M , rate = k9\*YM

v10: Y -> Z , rate = k10\*Y

v11: External -> External , rate = k11

vout12: Z -> , rate = k12\*Z

vout13: C -> , rate = k13\*C

vout14: B -> , rate = k13\*0.5\*B

vout15: Y -> , rate = k13\*0.5\*Y

#rates

k1 = 1

k2 = 1

k3 = 1

k4 = 0.5

k5 = 2

k6 = 1

k7 = 1

k8 = 1

k9 = 0.1

k10 = 1

k11= 0

k12= 1

k13= 1

#initial conditions

init: (M = 1, External = 0)

#init: (A= 1.0000000000000002, C= 0.5389278074441175, B= 0.922144385112478, YM= 0.0, BM= 0.2694639037219322, M= 0.7305360962780679, Y= 0.6666666666666671, X= 1.0000000000000002, Z= 0.6666666666666773, External = 1)

#Type II B

#reactions

vin1 : -> A , rate = k1

v2 : A -> B , rate = k2\*A

v3 : B + M -> BM , rate = k3\*B\*M

v4 : BM -> B + M , rate = k4\*BM

v5 : BM -> C + M , rate = k5\*BM

vin6 : -> X , rate = k6

v7 : X -> Y , rate = k7\*X

v8 : Y -> Z , rate = k8\*Y\*(1/(1+1000\*M))

v11: A + B -> AB , rate = k11\*A\*B\*step(t, 5000, 1)

v12: AB -> A + B , rate = k12\*AB

vout13: Z -> , rate = k13\*Z

vout14: C -> , rate = k14\*C

#rates

k1 = 1

k2 = 1

k3 = 1

k4 = 0.1

k5 = 1

k6 = 1

k7 = 1

k8 = 1

k11= 1

k12= 0.01

k13= 1

k14= 1

#initial conditions

init: (M = 1)

# Type II C

#reactions

vin1 : -> A , rate = k1

v2 : A -> B , rate = k2\*A

v3 : B + M -> BM , rate = k3\*B\*M

v4 : BM -> B + M , rate = k4\*BM

v5 : BM -> C + M , rate = k5\*BM

vin6 : -> X , rate = k6

v7 : X -> Y , rate = k7\*X

v8 : Y + M -> YM , rate = k8\*Y\*M\*(1+100\*YM\*step(t, 1000, 1))

v15: YM -> Y + M , rate = k15\*YM

v9 : Y -> Z , rate = k9\*Y

v10: X -> Y , rate = k10\*X

vout13: Z -> , rate = k13\*Z

vout14: C -> , rate = k14\*C

#rates

k1 = 1

k2 = 1

k3 = 1

k4 = 0.1

k5 = 1

k6 = 0.1

k7 = 1

k8 = 10

k9 = 1

k10= 1

k13= 1

k14= 1

k15 = 0.1

#initial conditions

init: (M = 1)

#Typ II D

#reactions

vin1 : -> A , rate = k1

v2 : A -> B , rate = k2\*A

v3 : B + M -> BM , rate = k3\*B\*M

v4 : BM -> B + M , rate = k4\*BM

v5 : BM -> C + M , rate = k5\*BM

vin10: -> X , rate = k10\*step(t, 100, 1)

v6 : X -> Y , rate = k6\*X

v7 : Y + M -> YM , rate = k7\*Y\*M

v8 : YM -> Y + M , rate = k8\*YM

v9 : Y -> Z , rate = k9\*YM

vout12: Z -> , rate = k12\*Z

vout13: C -> , rate = k13\*C

#rates

k1 = 1

k2 = 1

k3 = 1

k4 = 0.5

k5 = 2

k6 = 1

k7 = 1

k8 = 0.1

k9 = 1

k10 = 1

k12= 1

k13= 1

#initial conditions

init: (M = 1)

#Typ III A

#reactions

vin1 : -> A , rate = k1

v2 : A -> B , rate = k2\*A

v5 : B -> C , rate = k5\*B\*(1/(1+100\*M))

vin6 : -> X , rate = k6

v7 : X + M -> XM , rate = k7\*X\*M\*External

v8 : XM -> X + M , rate = k8\*XM

v9 : XM -> Z + M , rate = k9\*XM

v11: External -> External , rate = k11

vout12: Z -> , rate = k12\*Z

vout13: C -> , rate = k13\*C

#rates

k1 = 1

k2 = 1

k5 = 1

k6 = 1

k7 = 1

k8 = 1

k9 = 1

k11= 0

k12= 1

k13= 1

#initial conditions

init: (M = 1, External = 0)

#init: ( External = 1, A= 0.9999999999588062, C= 0.09326142322644992, B= 94.26142322432062, XM= 0.0, M= 1.0, X= 100.0, Z= 0.0)

# Typ III B

#reactions

vin1 : -> A , rate = k1

v2 : A -> B , rate = k2\*A

v3 : B + M -> BM , rate = k3\*B\*M

v4 : BM -> B + M , rate = k4\*BM

v5 : B -> C , rate = k5\*B

vin6 : -> X , rate = k6

v7 : X -> Y , rate = k7\*X

v8 : Y + M -> YM , rate = k8\*Y\*M

v9 : YM -> Y + M , rate = k9\*YM

v10: YM -> Z + M , rate = k10\*YM

vout13: Z -> , rate = k13\*Z

vout14: C -> , rate = k14\*C

v15: A + B -> AB , rate = k15\*A\*B\*step(t, 1000, 1)

#rates

k1 = 1

k2 = 1

k3 = 1

k4 = 1

k5 = 1

k6 = 1

k7 = 1

k8 = 1

k9 = 1

k10= 1

k11= 1

k13= 1

k14= 1

k15 = 1

#initial conditions

init: (M = 1)

# Typ III C

#reactions

vin1 : -> A , rate = k1

v2 : A -> B , rate = k2\*A

v5 : B -> C , rate = k5\*B\*(1/(1+10\*M))

vin6 : -> X , rate = k6

v7 : X -> Y , rate = k7\*X

v8 : Y + M -> YM , rate = k8\*Y\*M+(1000\*M\*step(t, 1200, 1))

v9 : YM -> Y + M , rate = k9\*YM

v10: YM -> Z + M , rate = k10\*YM

vout13: Z -> , rate = k13\*Z

vout14: C -> , rate = k14\*C

#rates

k1 = 0.8

k2 = 1

k3 = 1

k4 = 1

k5 = 1

k6 = 1

k7 = 1

k8 = 100

k9 = 0.1

k10= 1

k11= 0.1

k13= 1

k14= 1

#initial conditions

init: (M = 1)

#Typ III D

#reactions

vin1 : -> A , rate = k1

v2 : A -> B , rate = k2\*A

v5 : B -> C , rate = k5\*B\*(1/(1+100\*M))

vin6 : -> X , rate = k6\*step(t, 1200, 1)

v15: X -> Y , rate = k15\*X

v7 : Y + M -> YM , rate = k7\*Y\*M

v8 : YM -> Y + M , rate = k8\*YM

v9 : YM -> Z + M , rate = k9\*YM

vout12: Z -> , rate = k12\*Z

vout13: C -> , rate = k13\*C

#rates

k1 = 1

k2 = 1

k5 = 1

k6 = 1

k7 = 1

k8 = 1

k9 = 1

k11= 0

k12= 1

k13= 1

k15 = 1

#initial conditions

init: (M = 1)

#Typ IV A

#reactions

vin1 : -> A , rate = k1

v2 : A -> B , rate = k2\*A

v3 : B + M -> BM , rate = k3\*B\*M\*(1-External)

v4 : BM -> B + M , rate = k4\*BM

v5 : B -> C , rate = k5\*B

vin6 : -> X , rate = k6

v7 : X + M -> XM , rate = k7\*X\*M\*External

v8 : XM -> X + M , rate = k8\*XM

v9 : X -> Y , rate = k9\*X

v10: Y -> Z , rate = k10\*Y

v11: External -> External , rate = k11

vout12: Z -> , rate = k12\*Z

vout13: C -> , rate = k13\*C

#rates

k1 = 1

k2 = 1

k3 = 1

k4 = 0.1

k5 = 1

k6 = 1

k7 = 1

k8 = 0.1

k9 = 1

k10= 1

k11= 0

k12= 1

k13= 1

#initial conditions

init: (M = 1, External = 0)

#init: (External = 1,A= 1.0, C= 1.0000000000020075, B= 1.0000000000004445, XM= 0.0, BM= 0.9090909090910354, M= 0.09090909090896498, Y= 1.0000000000000007, X= 1.0, Z= 1.0000000000000135)

#Typ IV B

#reactions

vin1 : -> A , rate = k1

v2 : A -> B , rate = k2\*A

v3 : B + M -> BM , rate = k3\*B\*M

v4 : BM -> B + M , rate = k4\*BM

v5 : B -> C , rate = k5\*B

vin6 : -> X , rate = k6

v7 : X + M -> XM , rate = k7\*X\*M

v8 : XM -> X + M , rate = k8\*XM

v9 : X -> Y , rate = k9\*X

v10: Y -> Z , rate = k10\*Y

vout12: Z -> , rate = k12\*Z

vout13: C -> , rate = k13\*C

v15: A + B -> AB , rate = k15\*A\*B\*step(t, 50, 1)

#rates

k1 = 1

k2 = 1

k3 = 1

k4 = 1

k5 = 1

k6 = 1

k7 = 1

k8 = 0.1

k9 = 1

k10= 1

k11= 0

k12= 1

k13= 1

k15=1

#initial conditions

init: (M = 1)

# Typ IV C

#reactions

vin1 : -> A , rate = k1

v2 : A -> B , rate = k2\*A

v3 : B + M -> BM , rate = k3\*B\*M

v4 : BM -> B + M , rate = k4\*BM

v5 : B -> C , rate = k5\*B

vin6 : -> X , rate = k6

v7 : X + M -> XM , rate = k7\*Y\*M+(1000\*M\*step(t, 50, 1))

v8 : XM -> X + M , rate = k8\*XM

v9 : X -> Y , rate = k9\*X

v10: Y -> Z , rate = k10\*Y

vout12: Z -> , rate = k12\*Z

vout13: C -> , rate = k13\*C

#rates

k1 = 1

k2 = 1

k3 = 1

k4 = 0.1

k5 = 1

k6 = 1

k7 = 1

k8 = 0.1

k9 = 1

k10= 1

k11= 0

k12= 1

k13= 1

#initial conditions

init: (M=1.0)

#Typ IV D

#reactions

vin1 : -> A , rate = k1

v2 : A -> B , rate = k2\*A

v3 : B + M -> BM , rate = k3\*B\*M

v4 : BM -> B + M , rate = k4\*BM

v5 : B -> C , rate = k5\*B

vin6 : -> X , rate = k6\*step(t, 50, 1)

v7 : M + Y -> YM , rate = k7\*Y\*M

v8 : YM -> Y + M , rate = k8\*YM

v9 : X -> Y , rate = k9\*X

v10: Y -> Z , rate = k10\*Y

vout12: Z -> , rate = k12\*Z

vout13: C -> , rate = k13\*C

#rates

k1 = 1

k2 = 1

k3 = 10

k4 = 0.1

k5 = 1

k6 = 1

k7 = 10

k8 = 0.1

k9 = 0.5

k10= 1

k11= 0

k12= 1

k13= 1

#initial conditions

init: (M=1.0)