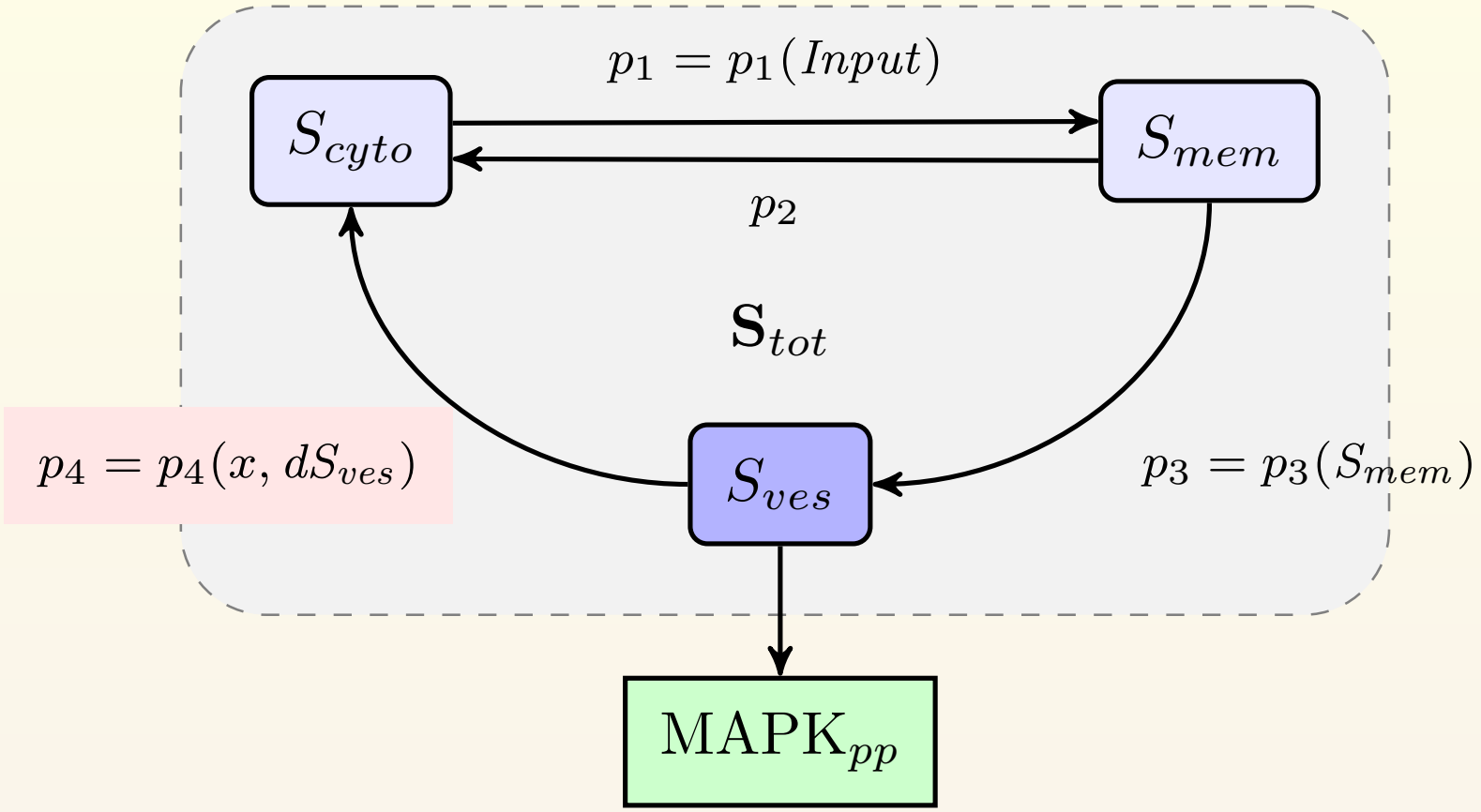
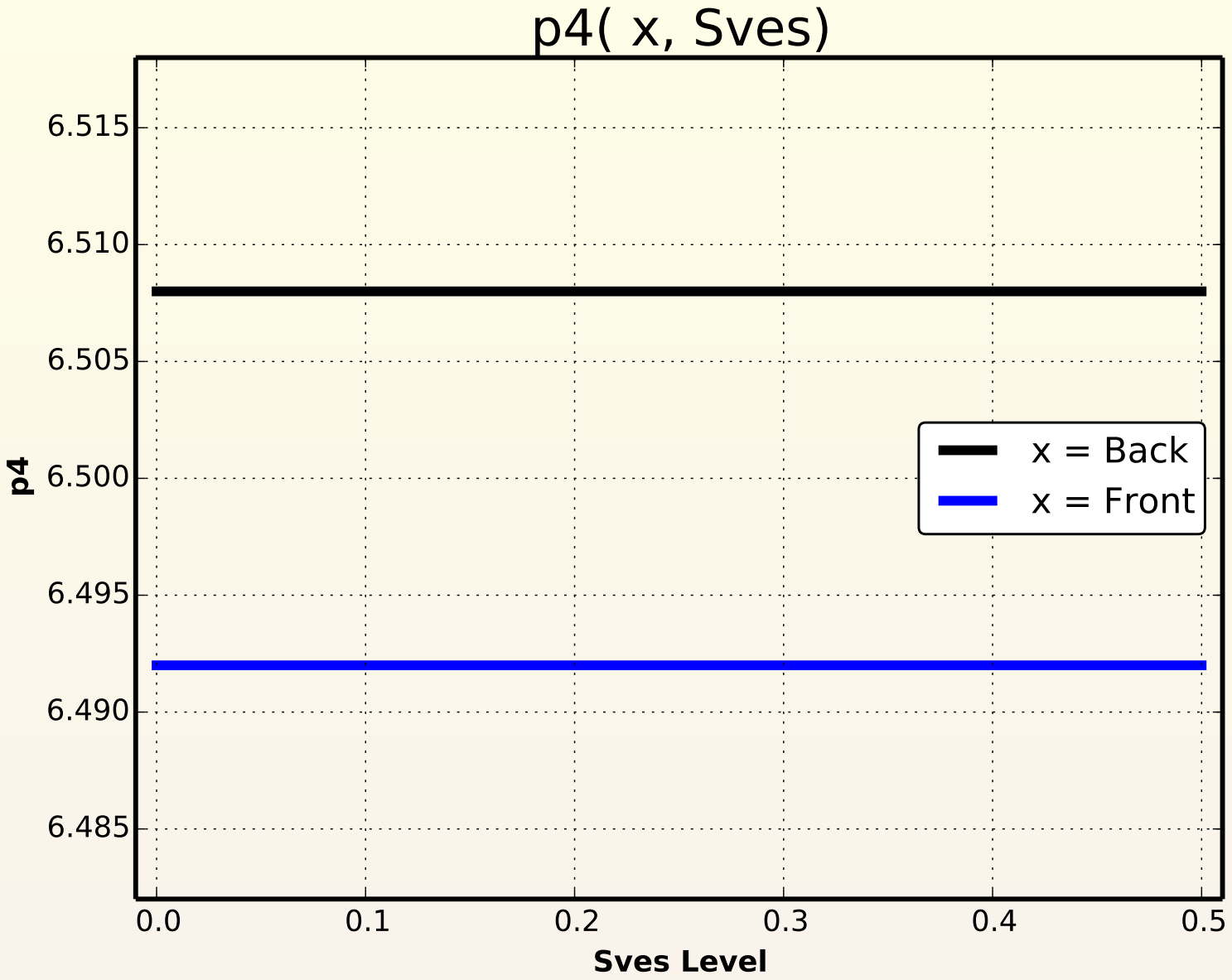
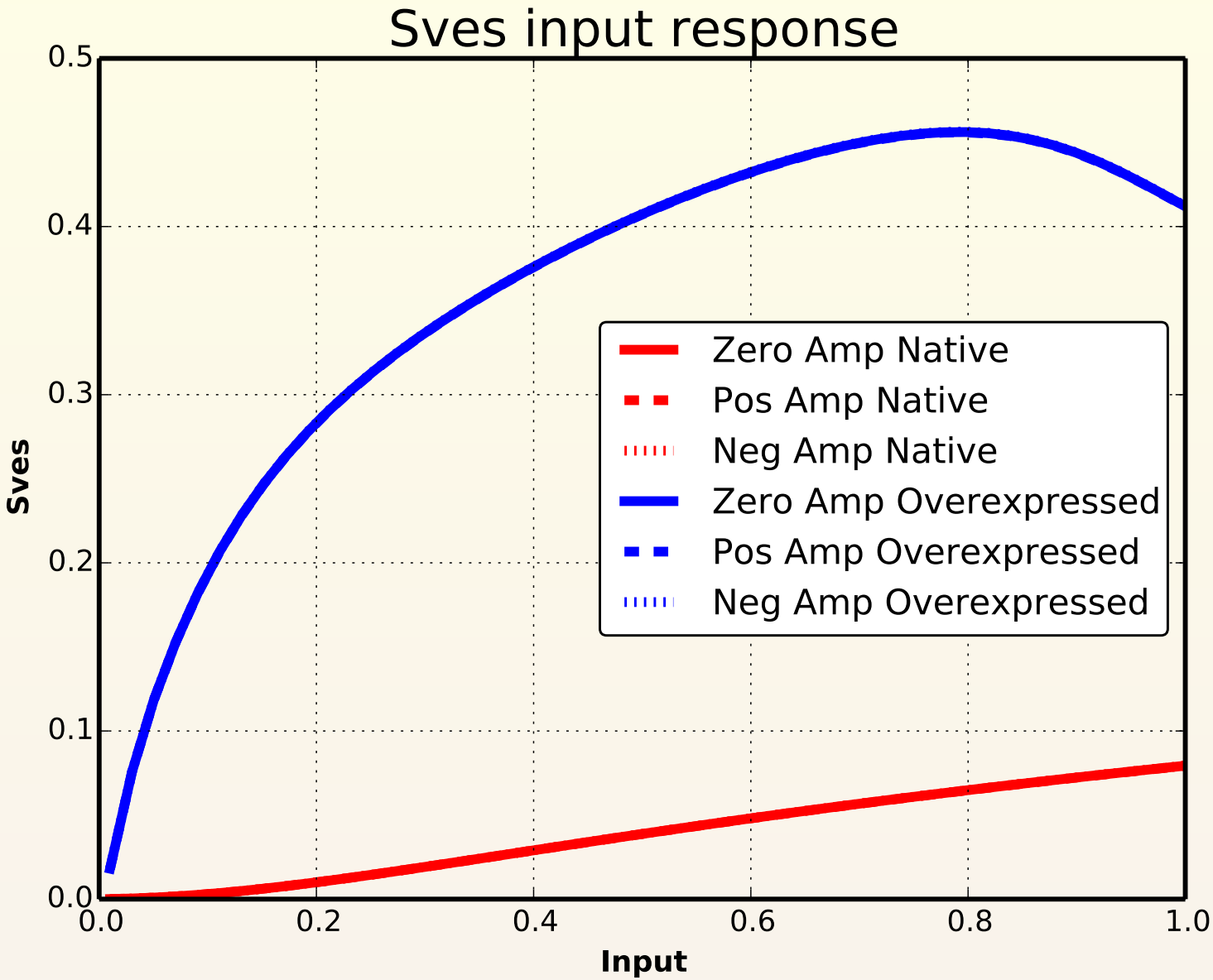
Model Schematic



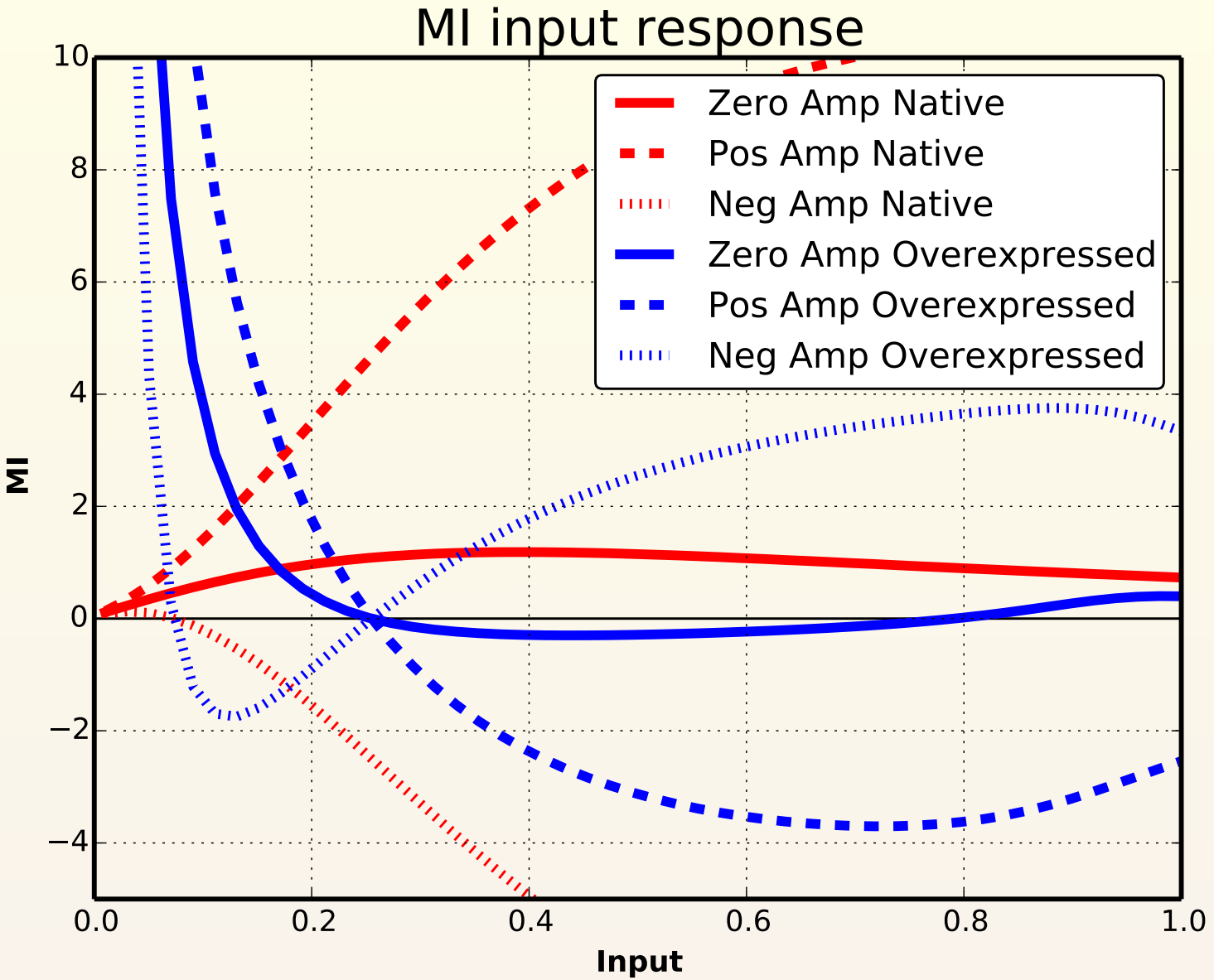
Constant p4


p4(x, Sves)
6.515
6.510
6.505
6.500
6.495
6.490
6.485
p4
0.0
0.1
0.2
0.3
0.4
0.5
Sves Level
x = Back
x = Front

Constant p4


Sves input response
Sves
Input
0.0
0.1
0.2
0.3
0.4
0.5
0.0
0.2
0.4
0.6
0.8
1.0
Zero Amp Native
Pos Amp Native
Neg Amp Native
Zero Amp Overexpressed
Pos Amp Overexpressed
Neg Amp Overexpressed

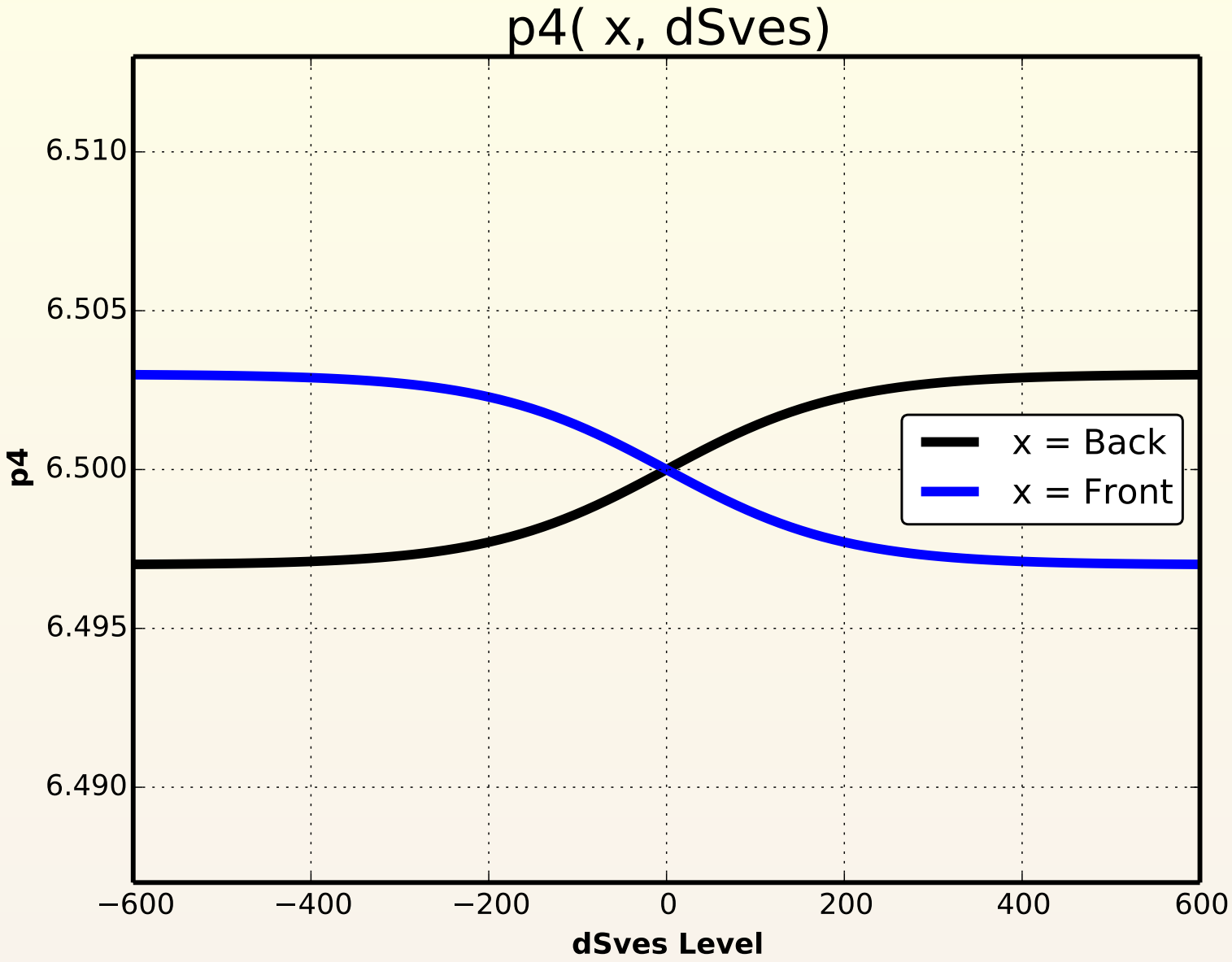
Constant p4


MI input response
Zero Amp Native
Pos Amp Native
Neg Amp Native
Zero Amp Overexpressed
Pos Amp Overexpressed
Neg Amp Overexpressed
MI
Input
10
8
6
4
2
0
−2
−4
0.0
0.2
0.4
0.6
0.8
1.0

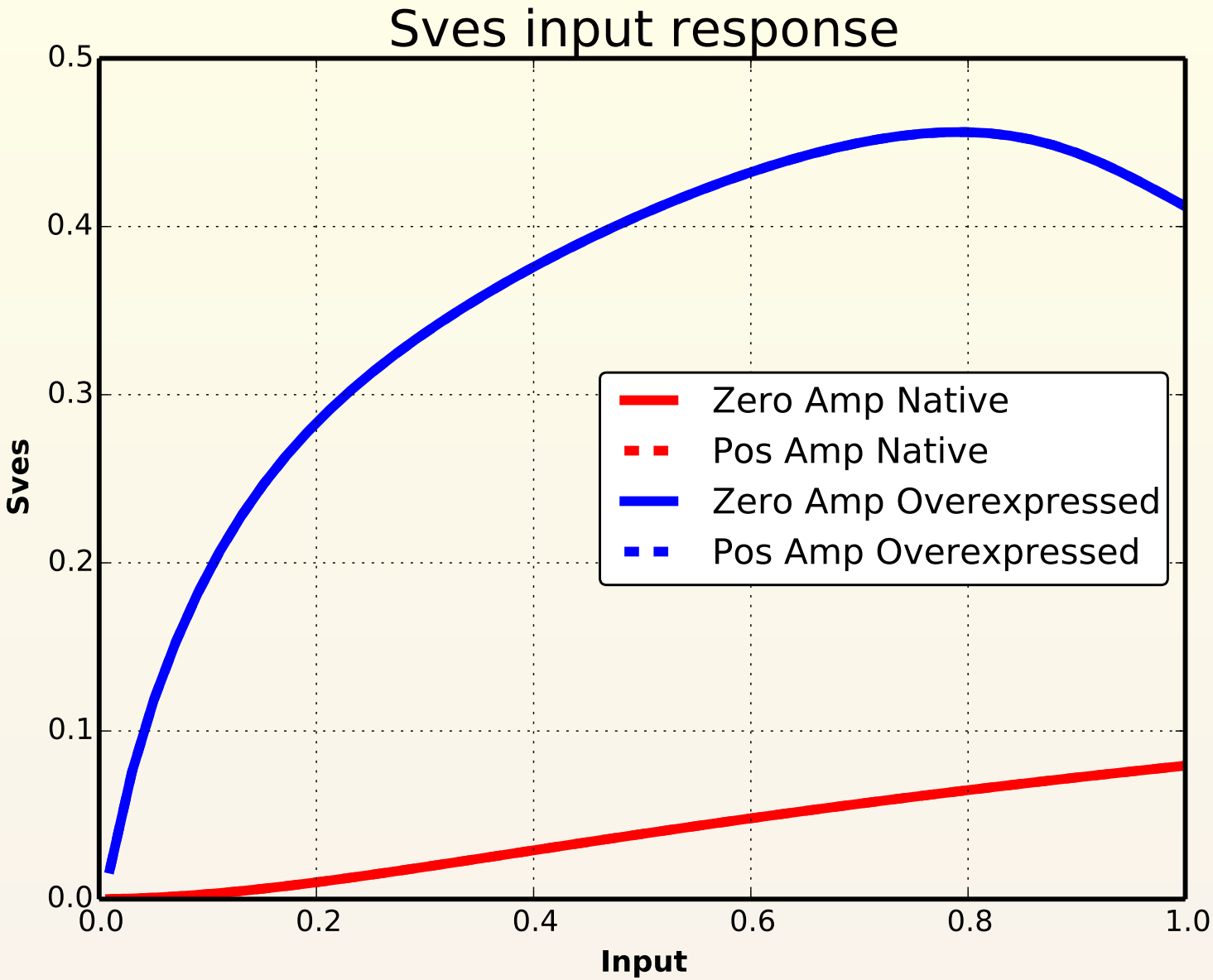
Constant p4

- Positive amp is good for native
- Negative amp is good for overexpressed
- Smoothly change amp w.r.t expression level

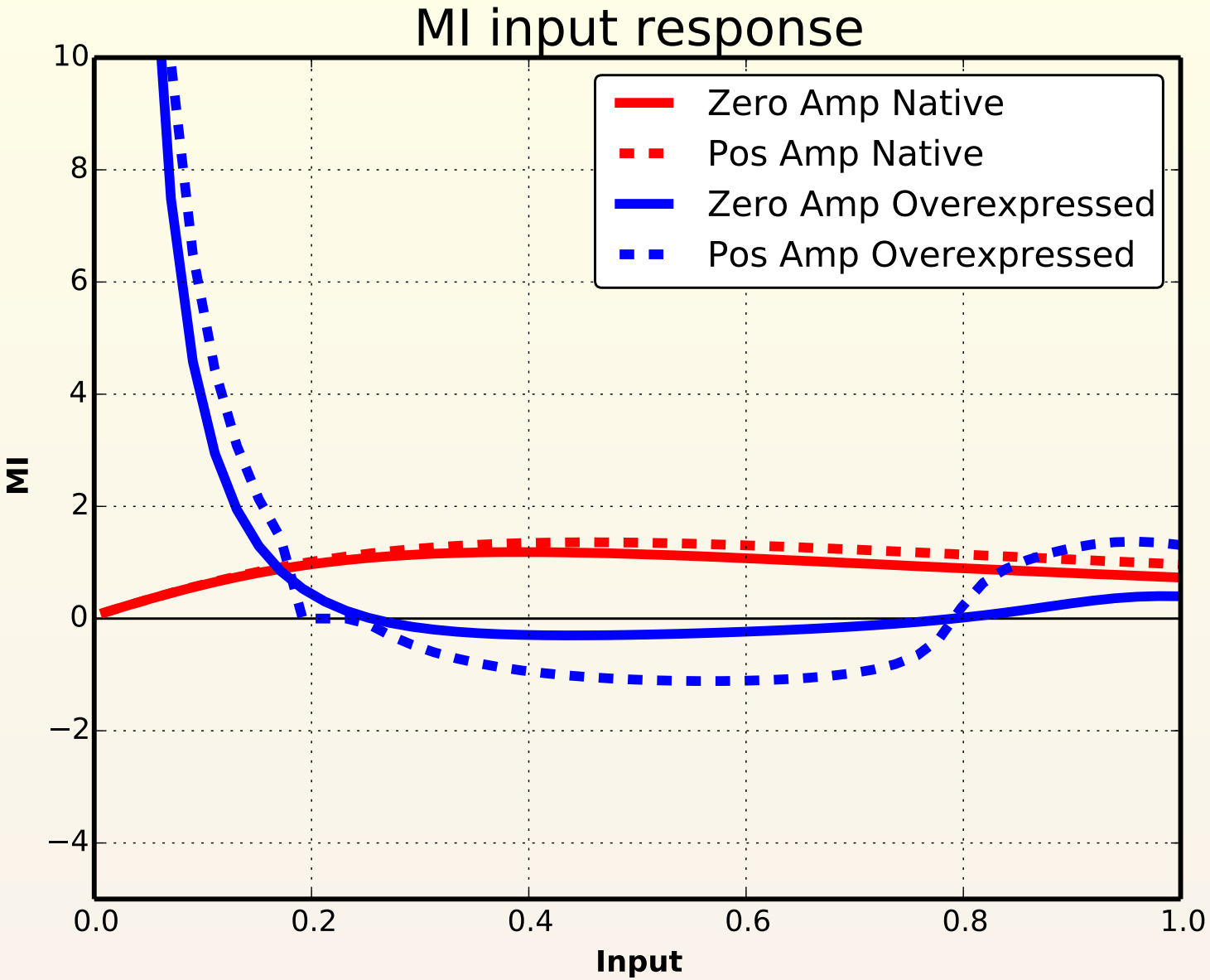
Coupled p4


p4(x, dSves)
6.510
6.505
6.500
6.495
6.490
p4
−600
−400
−200
0
200
400
600
dSves Level
x = Back
x = Front

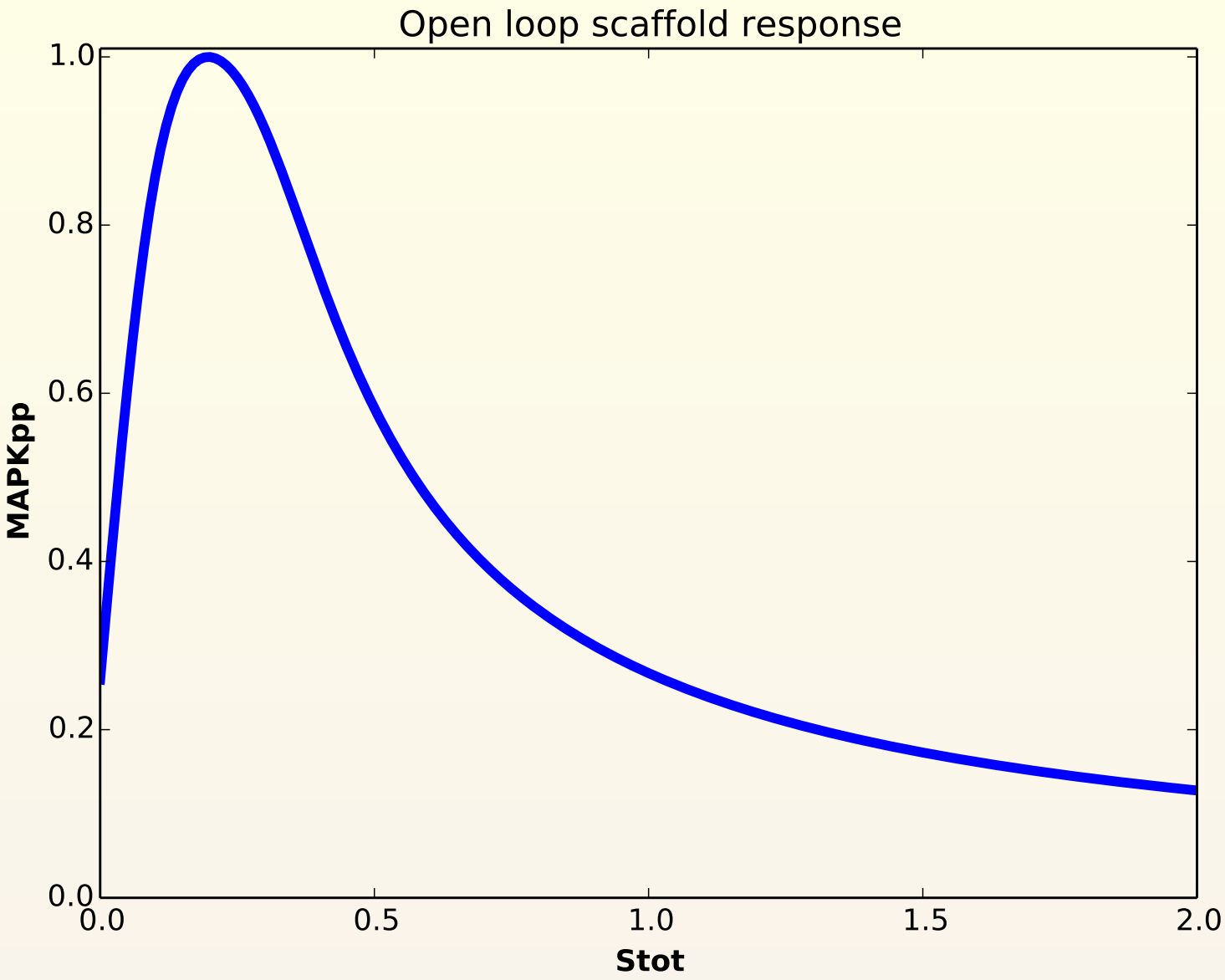
Coupled p4

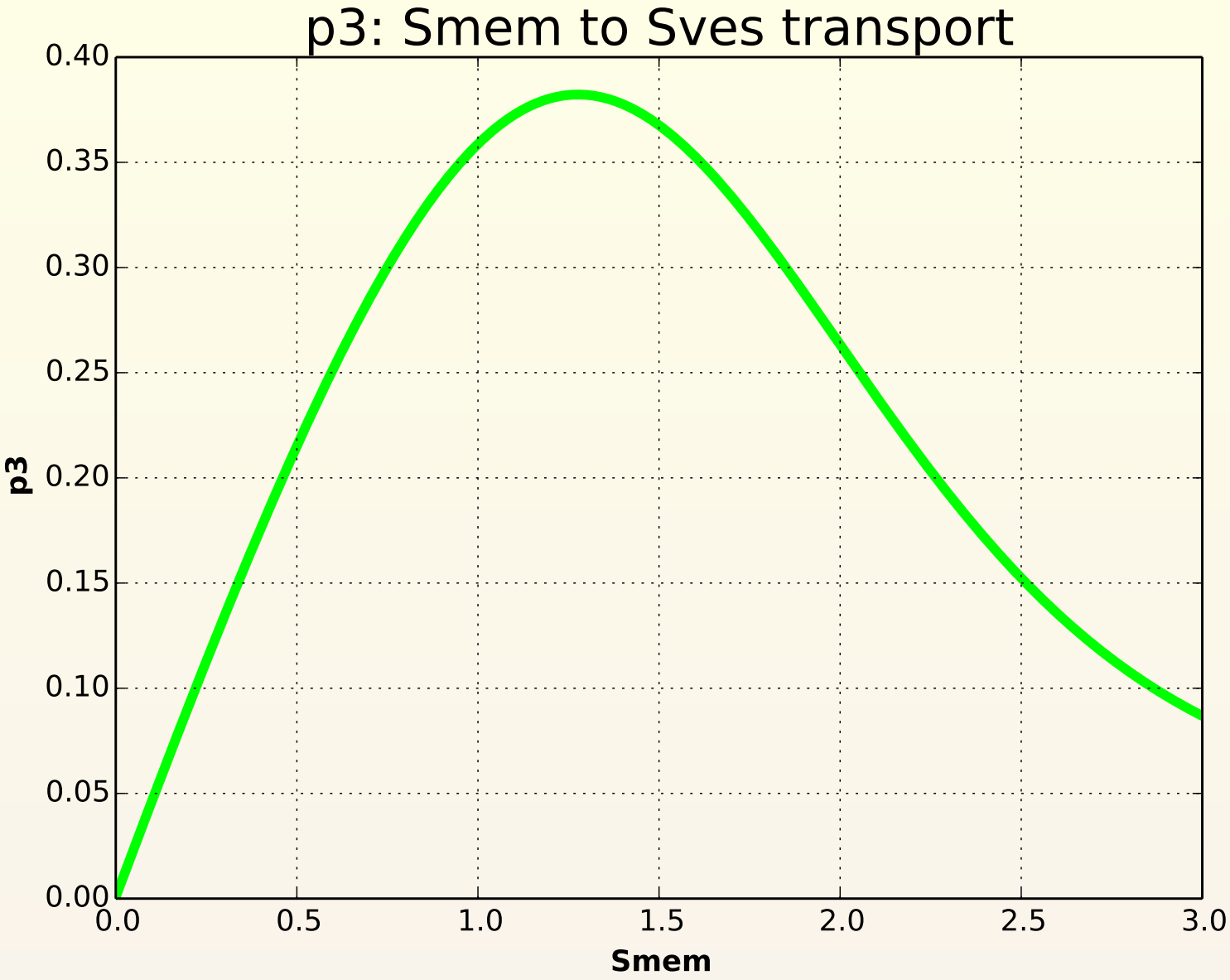

Sves input response
Sves
Input
0.0
0.1
0.2
0.3
0.4
0.5
0.0
0.2
0.4
0.6
0.8
1.0
Zero Amp Native
Pos Amp Native
Zero Amp Overexpressed
Pos Amp Overexpressed

Coupled p4

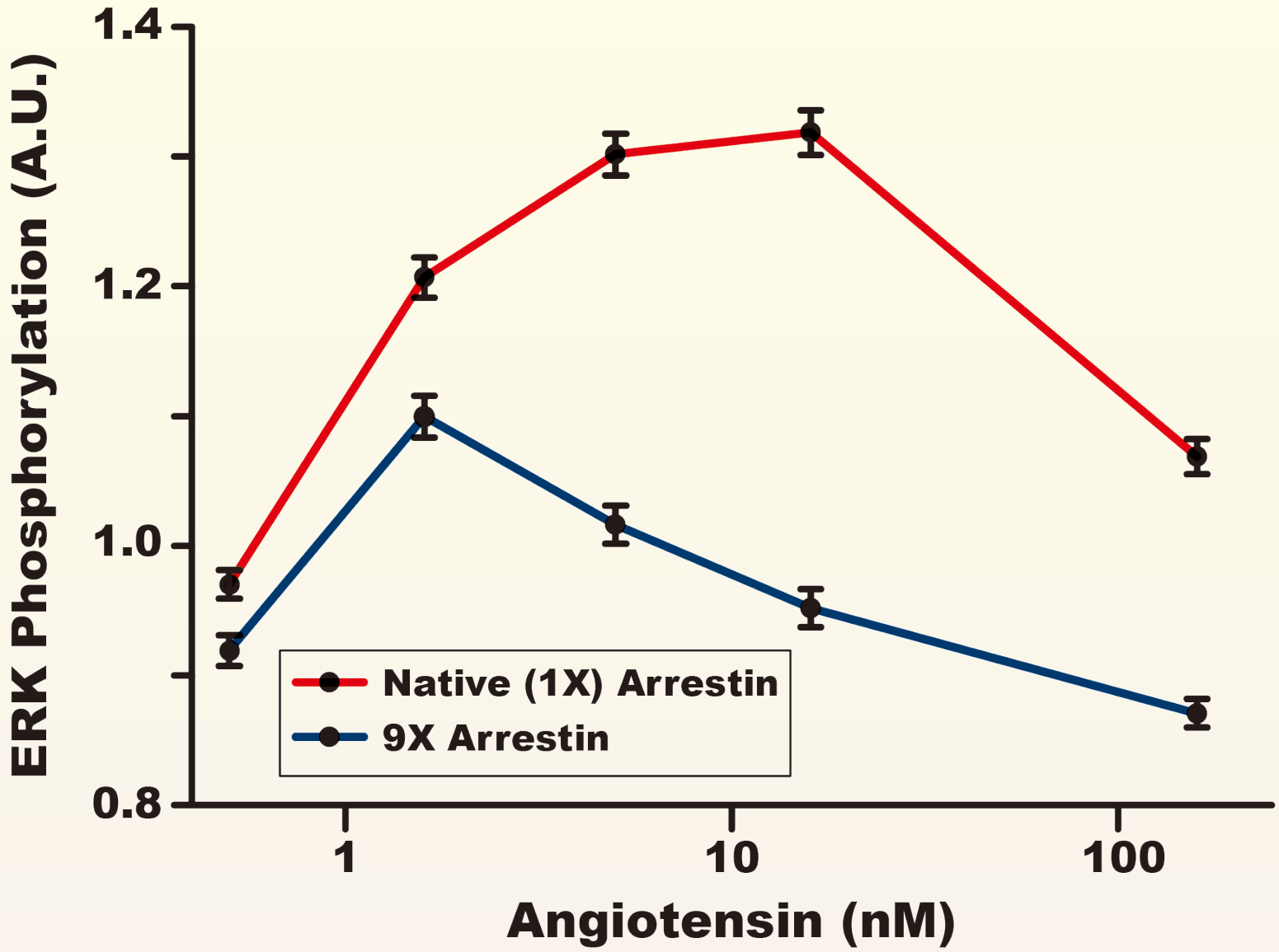

MI input response
Zero Amp Native
Pos Amp Native
Zero Amp Overexpressed
Pos Amp Overexpressed
MI
Input
10
8
6
4
2
0
−2
−4
0.0
0.2
0.4
0.6
0.8
1.0

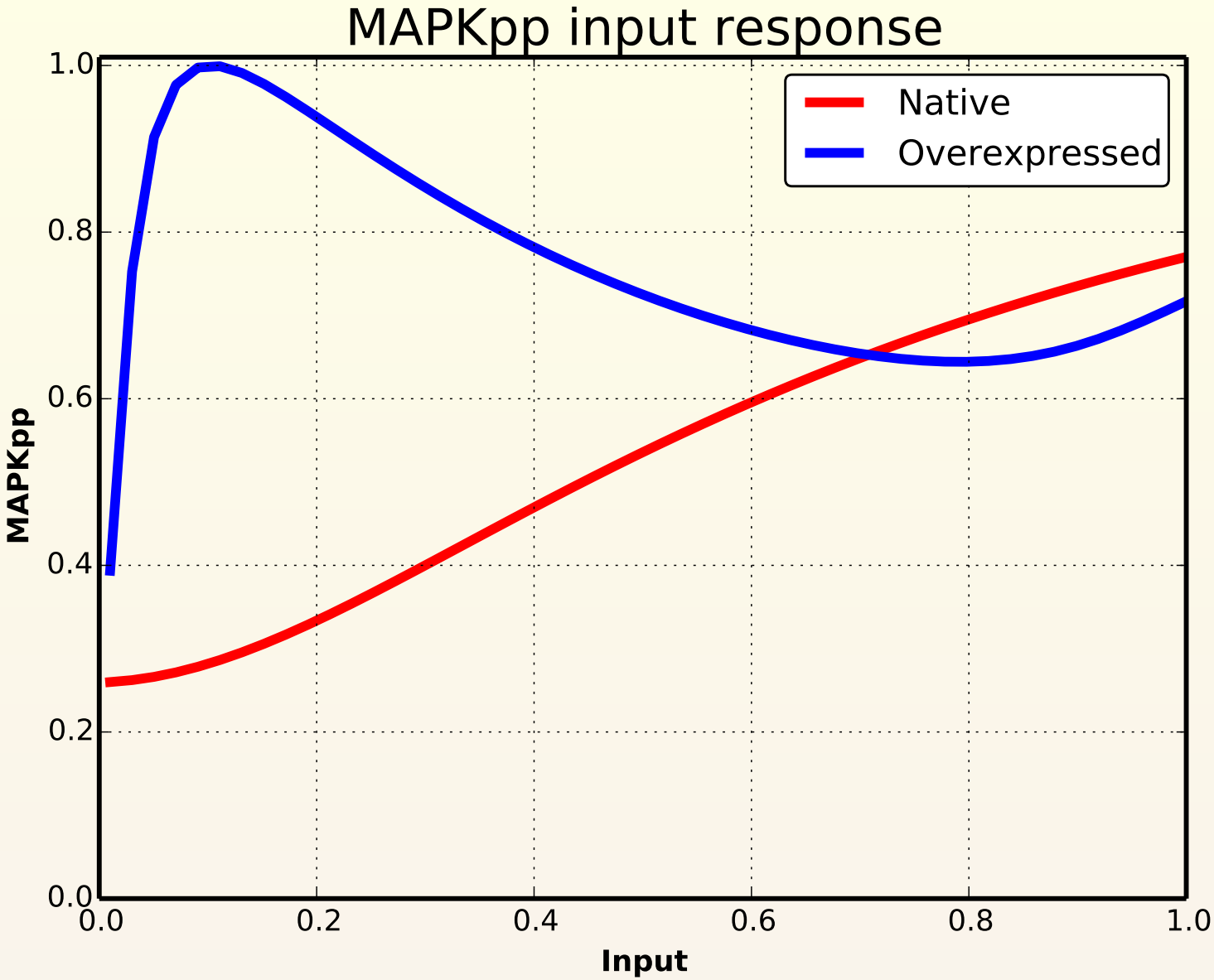
Comparison with experiments


Open loop scaffold response
MAPKpp
Stot
0.0
0.2
0.4
0.6
0.8
1.0
0.0
0.5
1.0
1.5
2.0

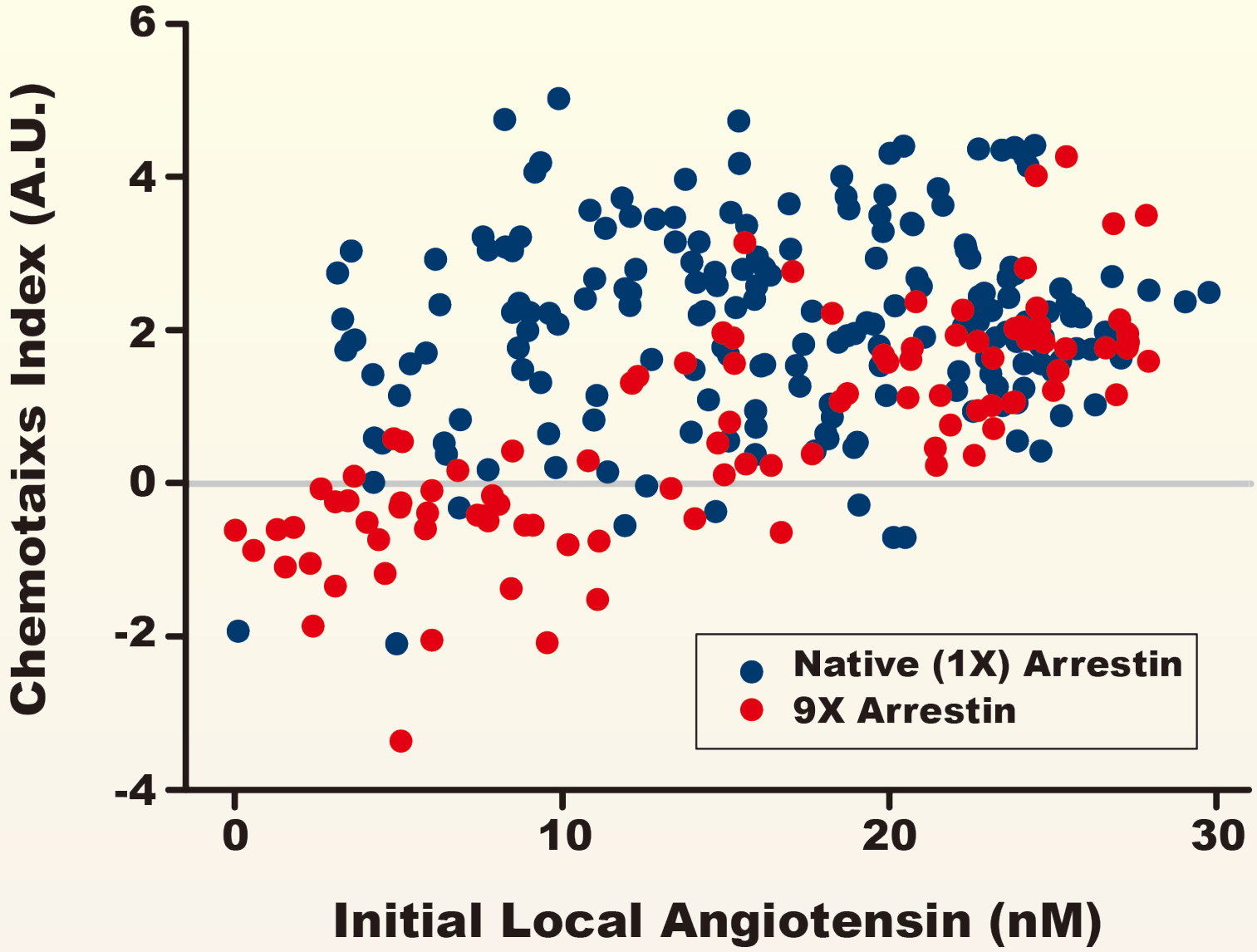

p3: Smem to Sves transport
0.40
0.35
0.30
0.25
0.20
0.15
0.10
0.05
0.00
p3
0.0
0.5
1.0
1.5
2.0
2.5
3.0
Smem

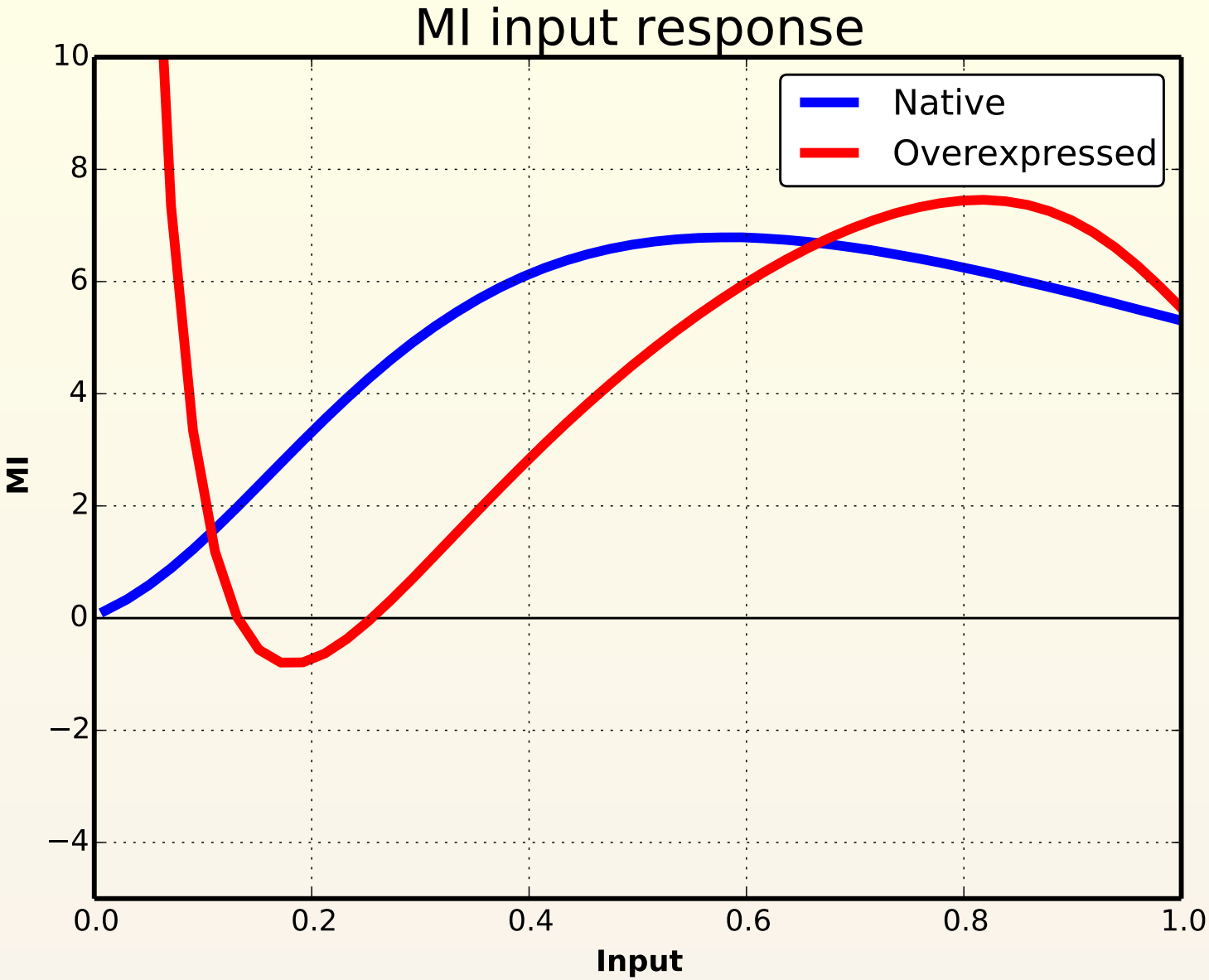
D

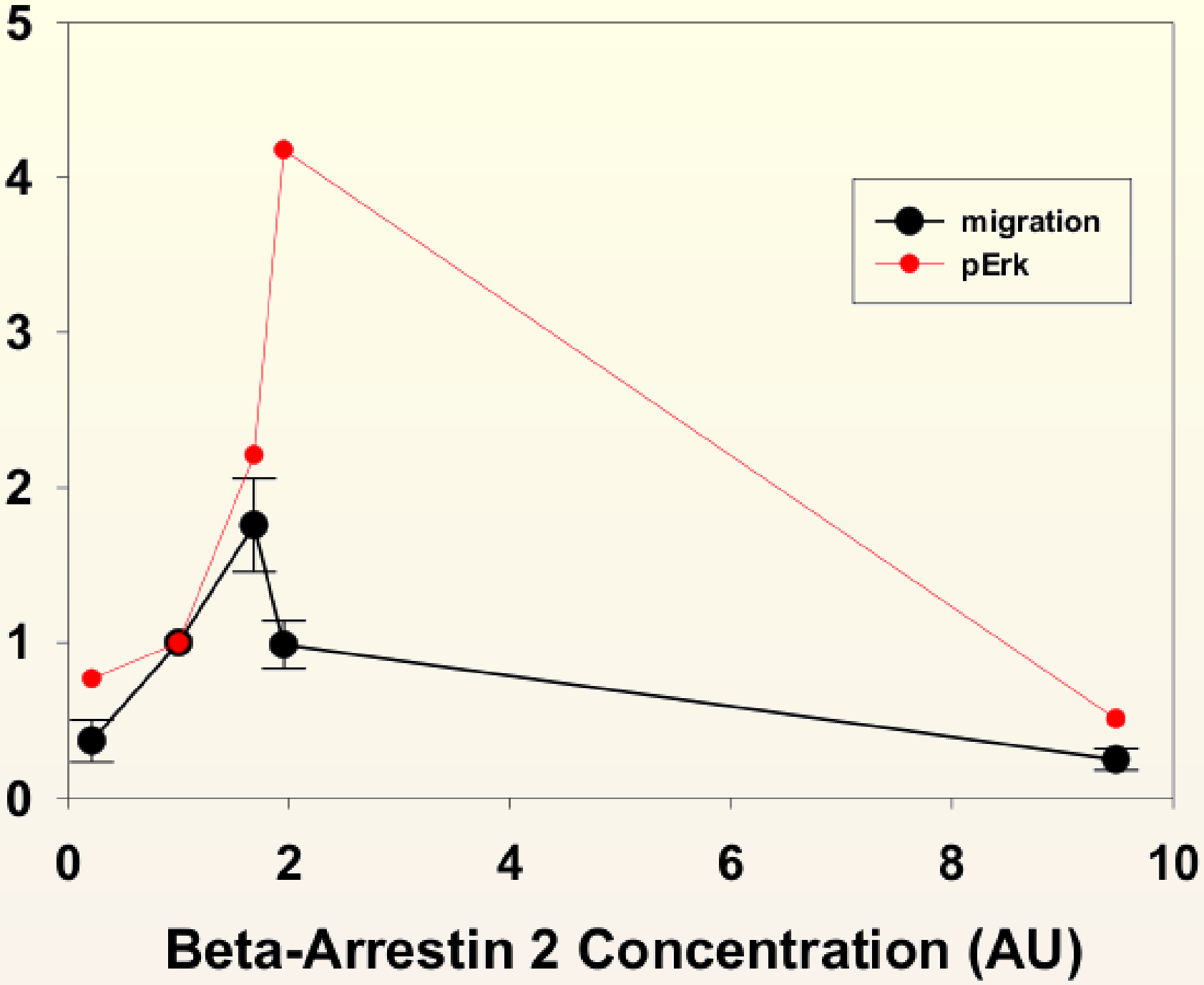

ERK Phosphorylation (A.U.)
1.4
1.2
1.0
0.8
1
10
100
Angiotensin (nM)
Native (1X) Arrestin
9X Arrestin

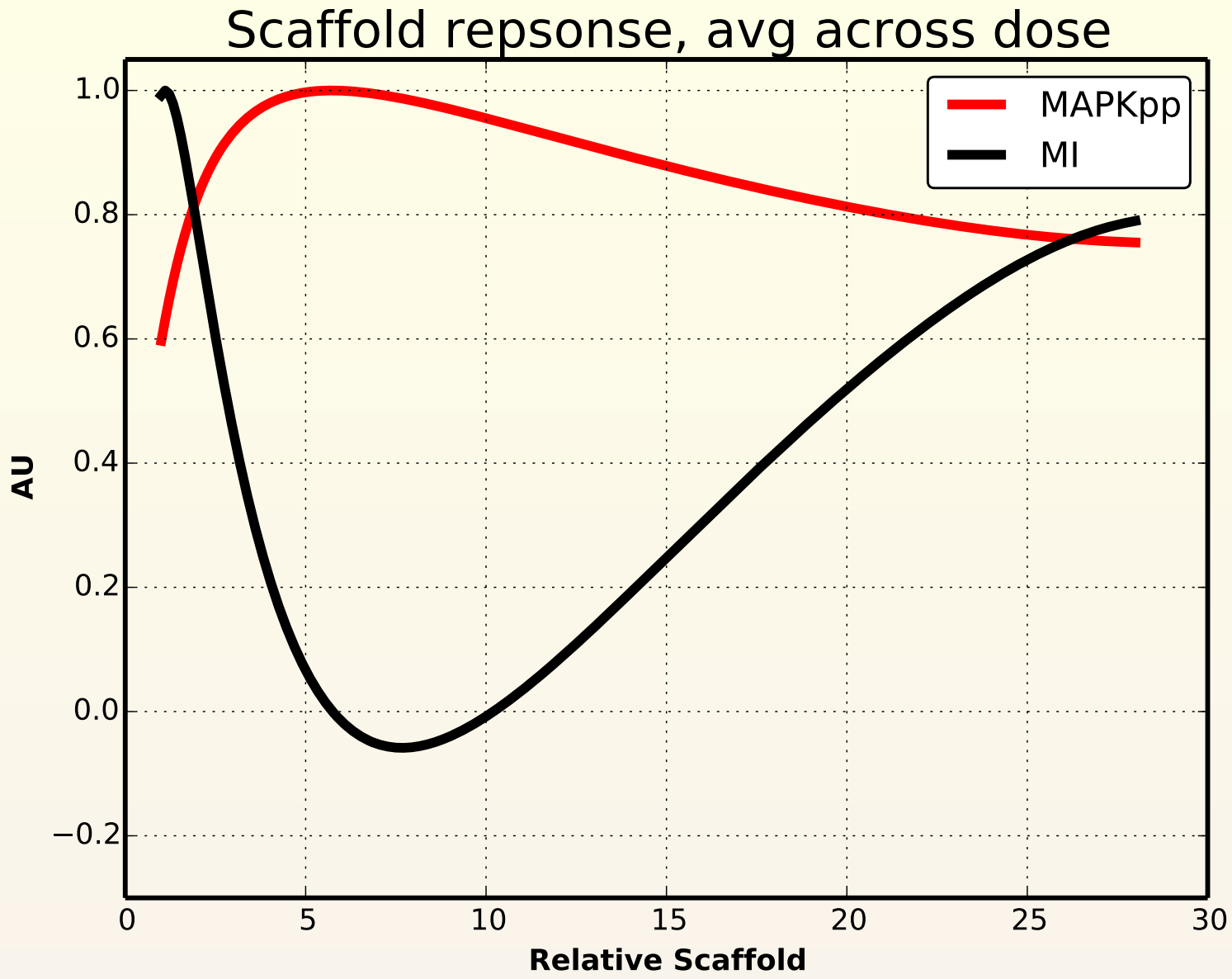

MAPKpp input response
Native
Overexpressed
MAPKpp
Input
0.0
0.2
0.4
0.6
0.8
1.0

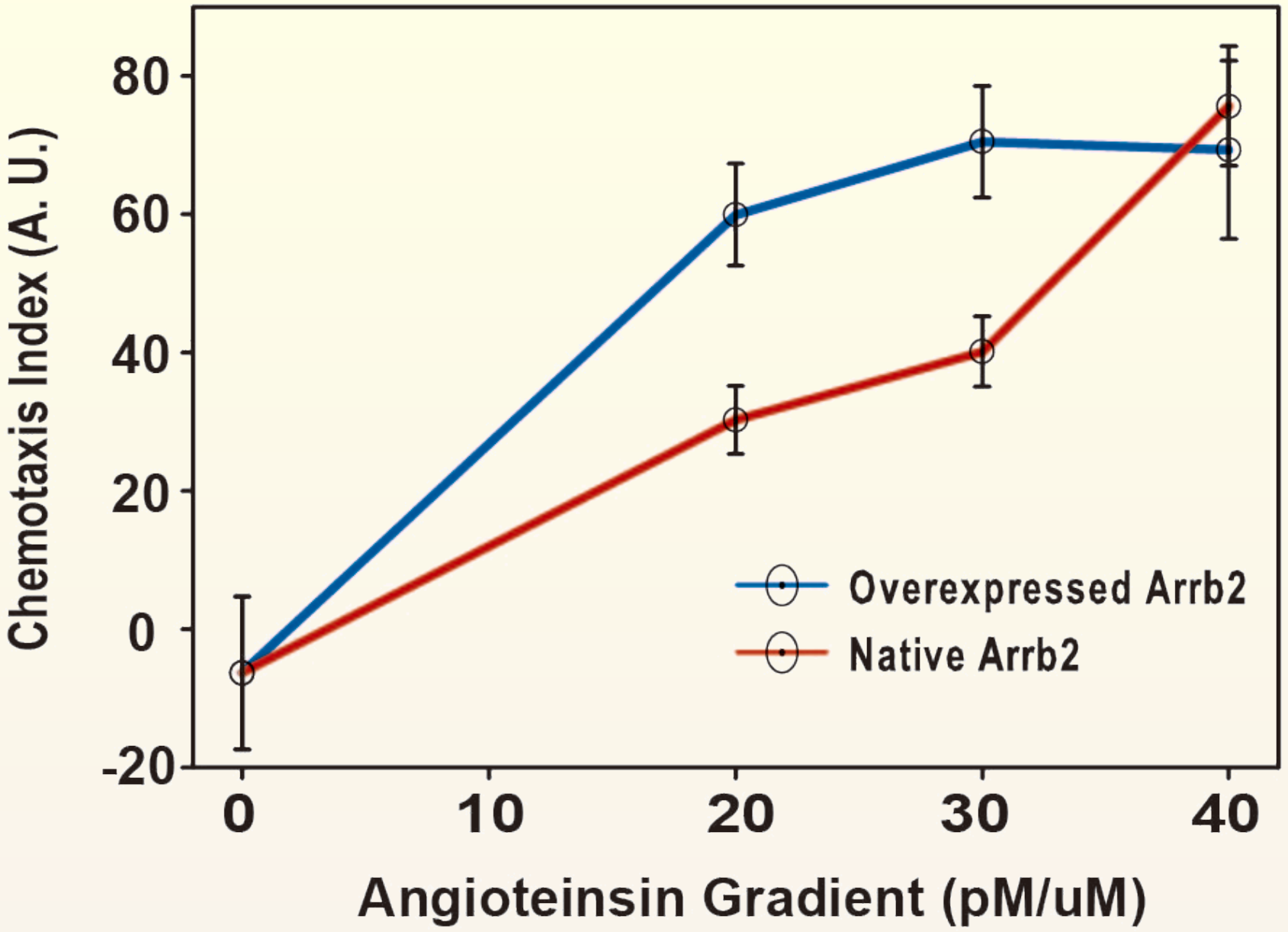
B

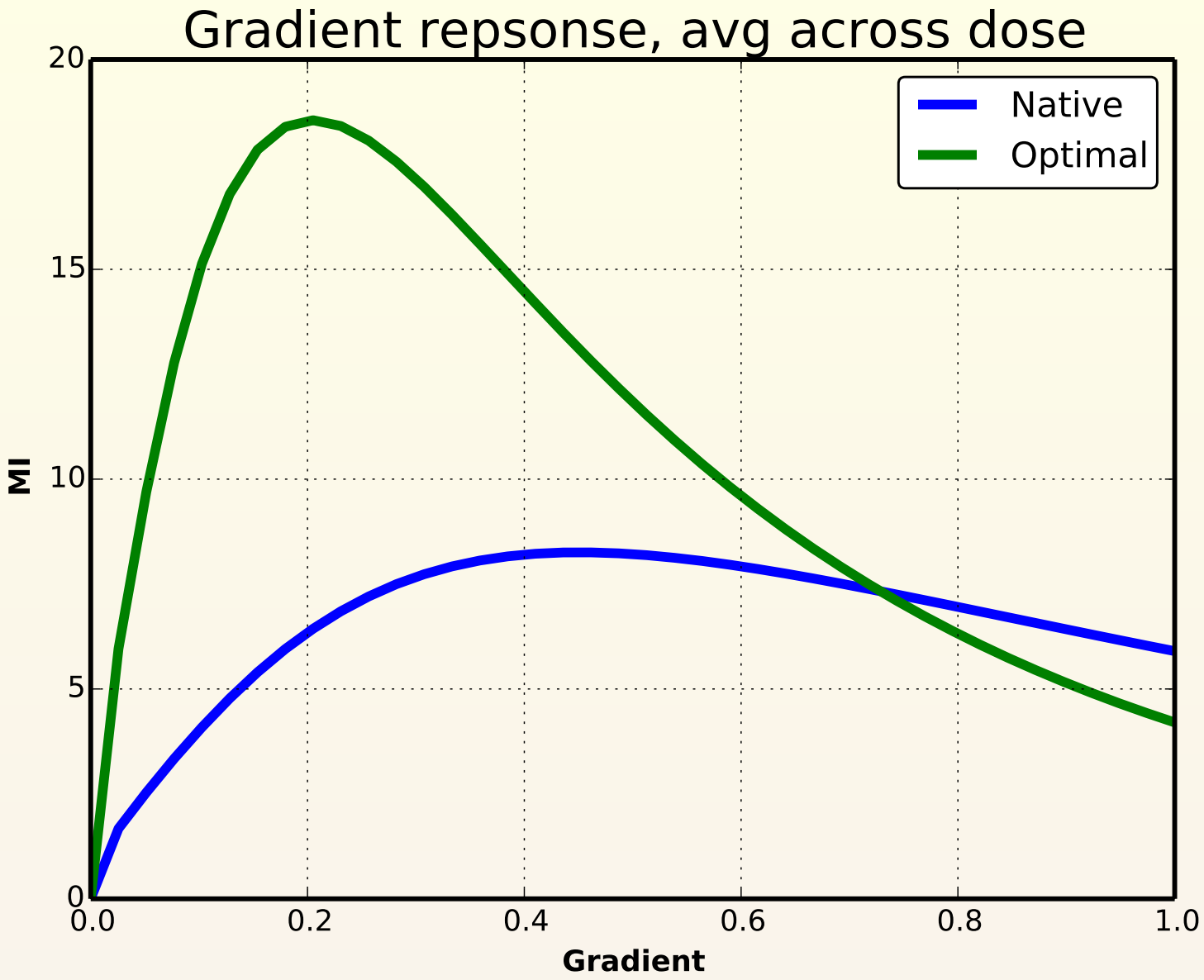

Chemotaixs Index (A.U.)
6
4
2
0
-2
-4
0
10
20
30
Initial Local Angiotensin (nM)
Native (1X) Arrestin
9X Arrestin


MI input response
Native
Overexpressed
MI
Input
10
8
6
4
2
0
−2
−4
0.0
0.2
0.4
0.6
0.8
1.0


5
4
3
2
1
0
0
2
4
6
8
10
migration
pErk
Beta-Arrestin 2 Concentration (AU)

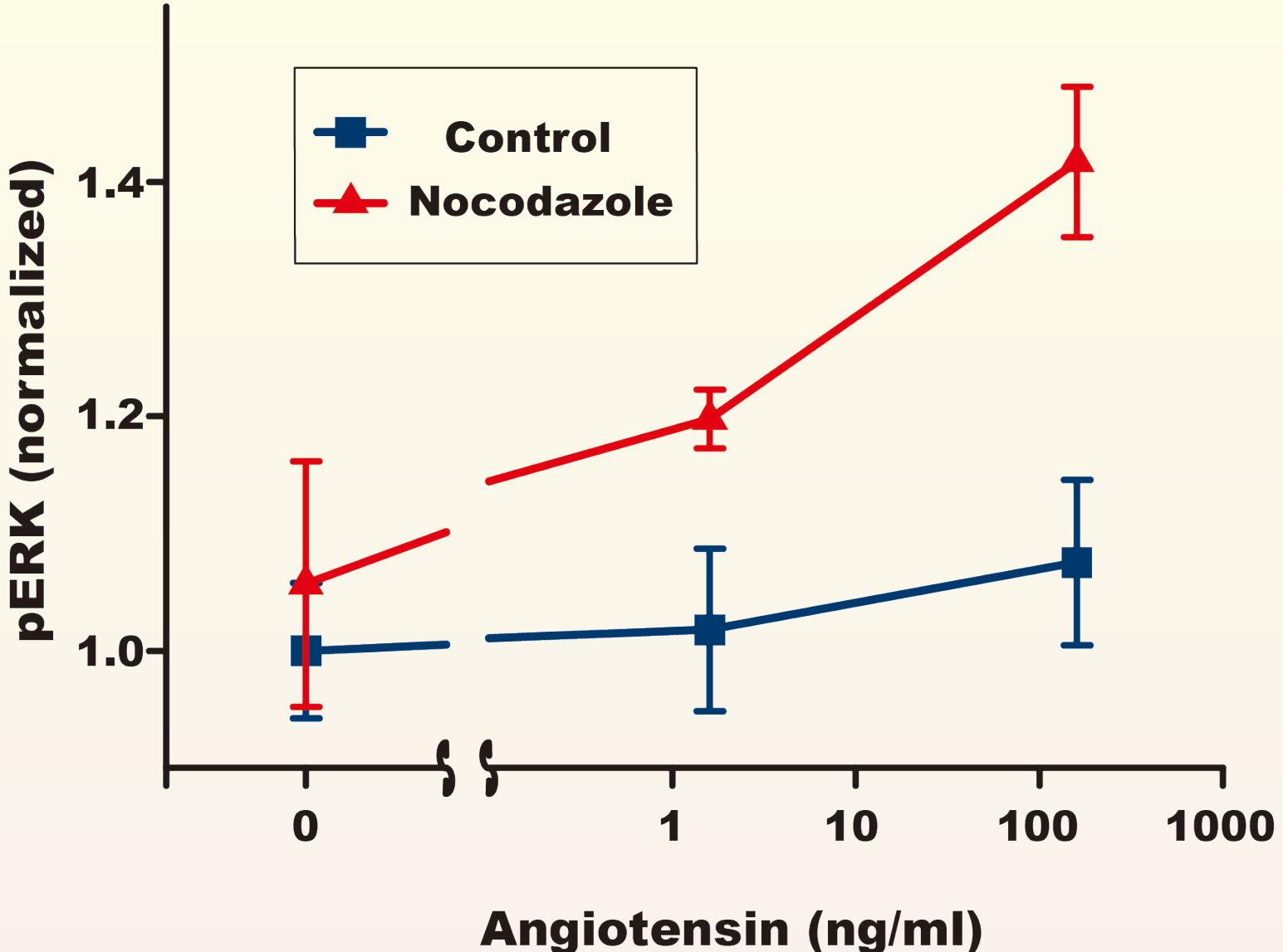

Scaffold repsonse, avg across dose
MAPKpp
MI
AU
1.0
0.8
0.6
0.4
0.2
0.0
−0.2
0
5
10
15
20
25
30
Relative Scaffold


Chemotaxis Index (A. U.)
80
60
40
20
0
-20
0
10
20
30
40
Angioteinsin Gradient (pM/uM)
Overexpressed Arrb2
Native Arrb2

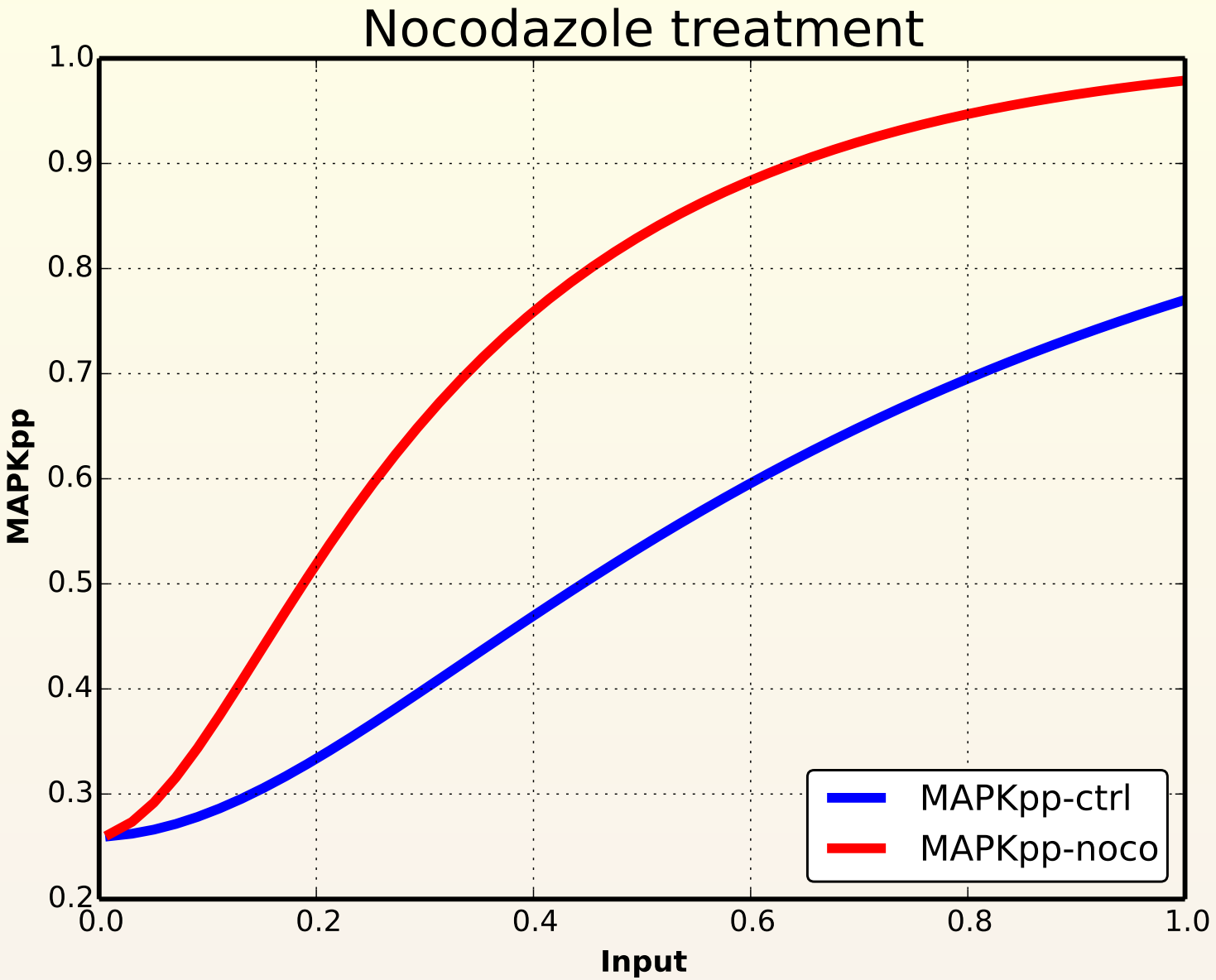

Gradient repsonse, avg across dose
Native
Optimal
MI
Gradient
0
5
10
15
20
0.0
0.2
0.4
0.6
0.8
1.0

Nocodazole treatment

E

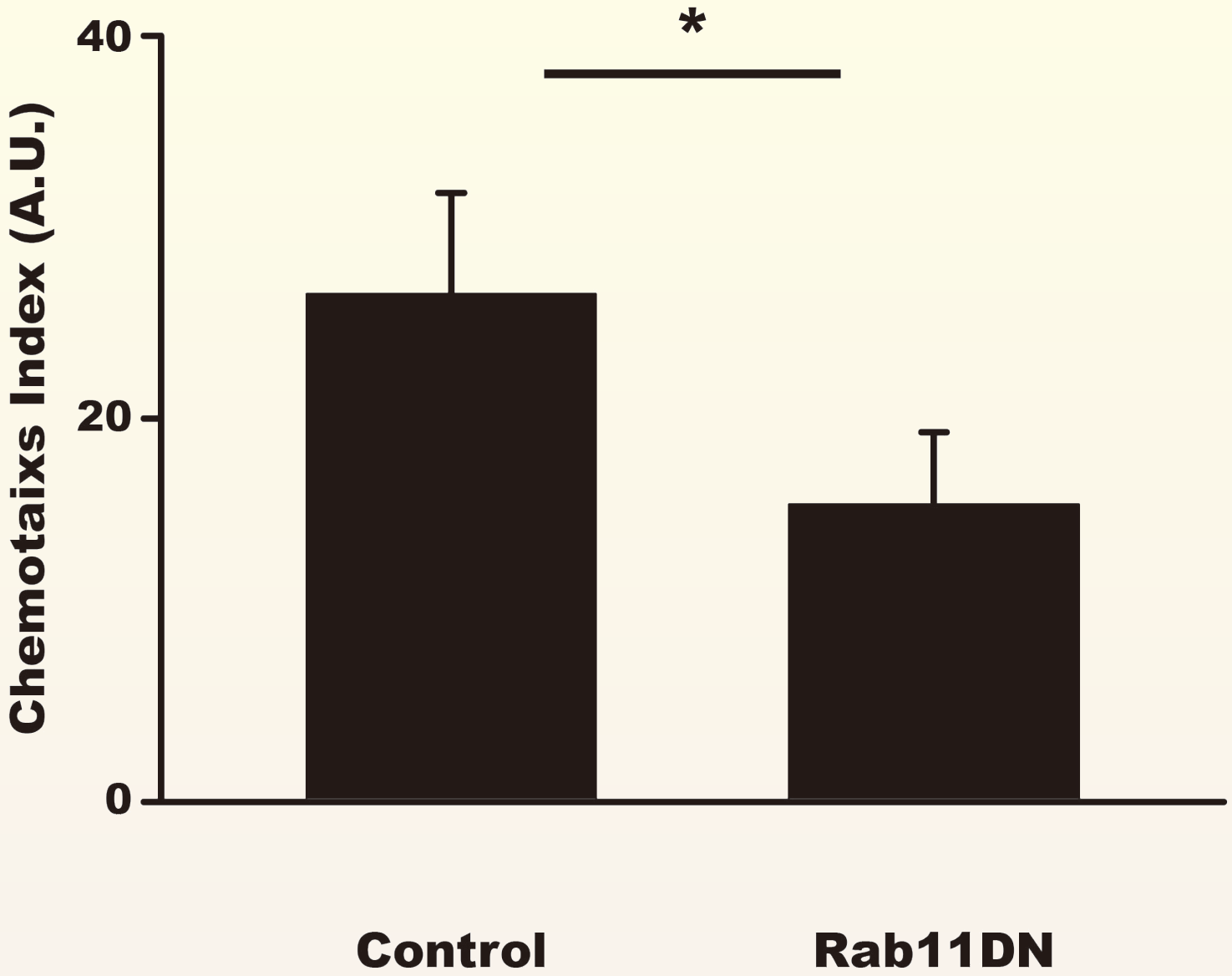


$S_{ves} \rightarrow S_{cyto}, 20\% p_4$

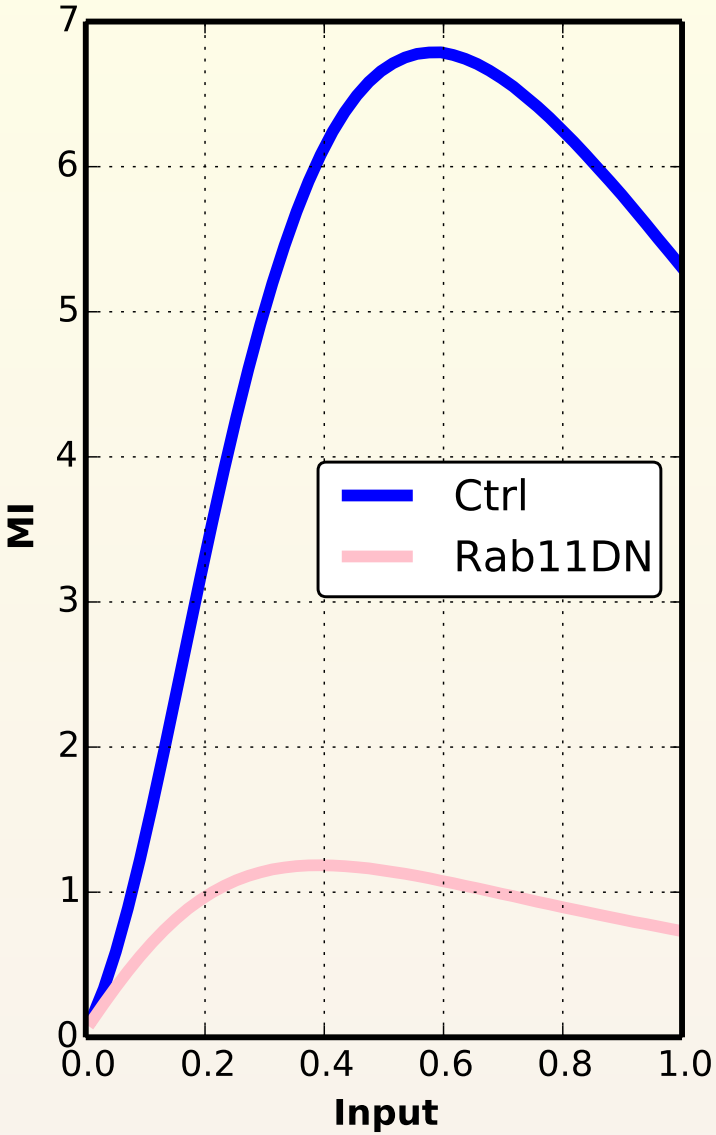


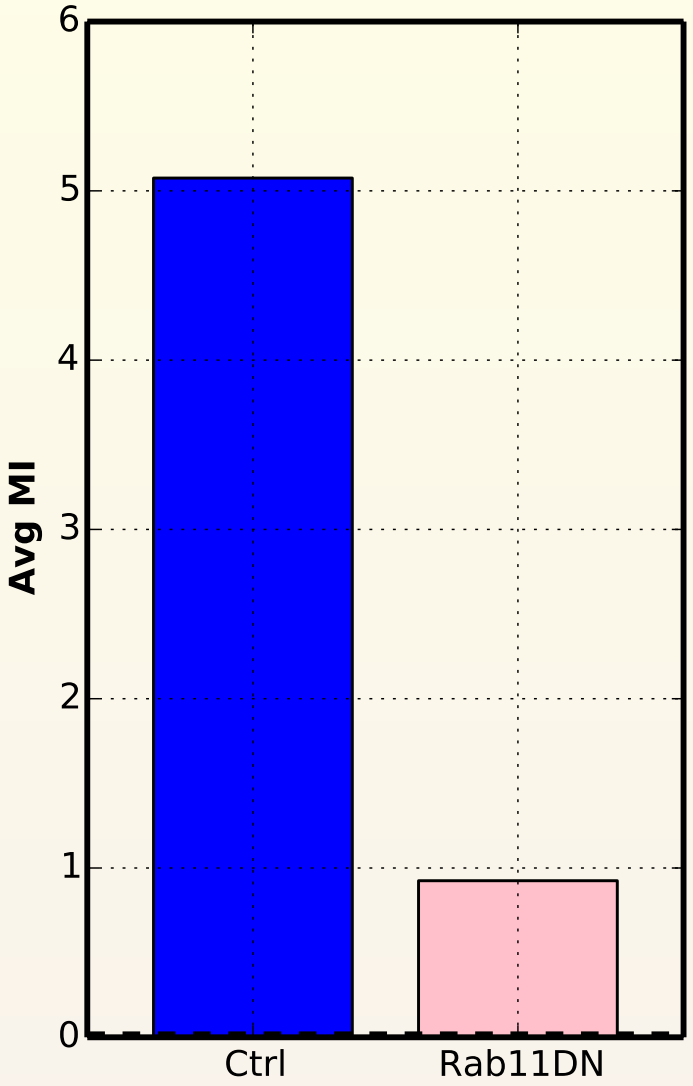
Rab11-DN

F



Rab11-DN


MI
Input
Ctrl
Rab11DN
0
1
2
3
4
5
6
7
0.0
0.2
0.4
0.6
0.8
1.0


Avg MI
Ctrl
Rab11DN
0
1
2
3
4
5
6