This is Supplementary data for Combinatorial bZIP dimers define complex DNA-binding specificity landscapes by José A. Rodríguez-Martínez, Aaron W. Reinke, Devesh Bhimsaria, Amy E. Keating, Aseem Z. Ansari 2017.

Supplementary file 2. MEME motifs and Sequence Specificity and Energy Landscapes (SEL) for human bZIP homodimers and heterodimers. **column 1**, bZIP dimer and dissociation constant of bZIP dimerization in the absence of DNA, from Reinke et al. (Science, 2013); **column 2**, Representative MEME motifs derived using the top 1,000 12-mer sequences ranked by CSI intensity; **column 3**, SEL displaying CSI intensities of 12-mer sequences in the 0-, 1-, 2- mismatch rings. Seed motifs used to draw SELs are shown on top; **column 4**, Box plot of CSI intensities corresponding to the first three rings (0-, 1-, 2-mismatch rings) of the SEL. bZIP heterodimer motifs were classified as Conjoined (C), Variably-spaced (V), or Emergent (E) based on the DNA binding preferences of the composing bZIPs and a notation of the category included between columns 2 and 3. Multiple MEME motifs were identified for some homodimers and heterodimers. In such cases, motifs are bracketed in column 1.

Homodimer (PPI, Kd)	MEME motif	Sequence Specificity & Energy Landscape (SEL)	Box plot for SEL rings
ATF2 (32 nM)	1 2 3 4 5 6 7 8 9 10	ATGACGTCAT	eu 200- V Z/X 150- U 100- U 1 2 2 Mismatch (Hamming Distance)
ATF3 (218 nM)		ATGACGTCAT	2000 J 1 2000 J
ATF4 (412 nM)	1 2 3 4 5 6 7 8 9 10	ATGACGTCAT	e 200
ATF6 (27 nM)	1 2 3 4 5 6 7 8 9 10	ATGACGTGGC	6000
ATF6 (27 nM)		ATGACGTCAT	e 600

ATF6B (<1 nM)



ATF6B (<1 nM)



BATF3 (128 nM)



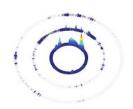
CEBPA (10 nM)



CEBPE (3 nM)



ATGACGTGGC

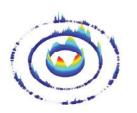


ATGACGTCAT

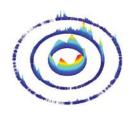




ATTGCGCAAT

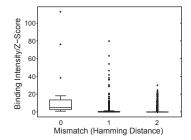


ATTGCGCAAT



I

0 1 2 Mismatch (Hamming Distance)



ATGACGTCAT



Binding Intensity/Z-Score 9 001170. T 0 1 2 Mismatch (Hamming Distance)

Binding Intensity/Z-Score 200 150 0 1 2 Mismatch (Hamming Distance)

Binding Intensity/Z-Score 160 140 120 100 80-60-40-20- \perp 0 1 2 Mismatch (Hamming Distance) **CEBPG** (<1 nM)



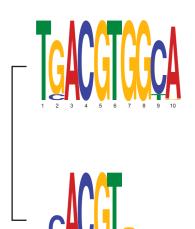
CREB1 (15 nM)



CREB3 (93 nM)

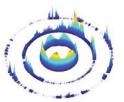


CREB3L1 (10 nM)

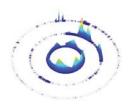


CREB3L1 (10 nM)





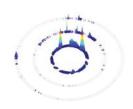
ATGACGTCAT

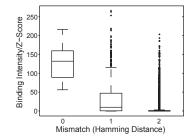


ATGACGTGGC



ATGACGTGGC





0 1 2 Mismatch (Hamming Distance)

Binding Intensity/Z-Score 0 1 2 Mismatch (Hamming Distance)

0 1 2 Mismatch (Hamming Distance) DBP (8 nM)



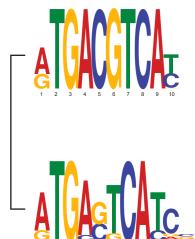
FOSL1 (>5000 nM)



HLF (3 nM)



JUN (314 nM)



JUN (314 nM)

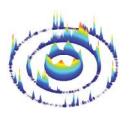




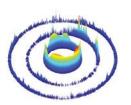
ATGACGTCAT



ATTACGTAAT



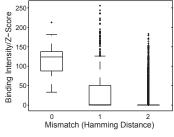
ATGACGTCAT



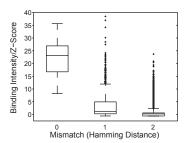
ATGAGTCAT



TACGTAAT 250 8 200 .



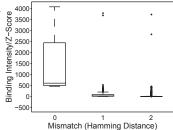
Budjud Judou Judou



 MAFB (62 nM) AA

TGCTGAGTCAGCA



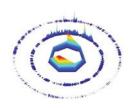


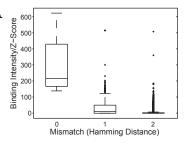
MAFG (15 nM)



MEME motif

TGCTGAGTCAGCA



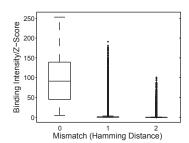


NFE2 (656 nM)



ATGAGTCAT

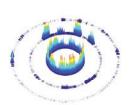


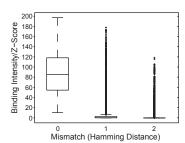


NFE2L1 (27 nM)



ATGAGTCAT

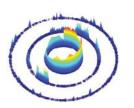


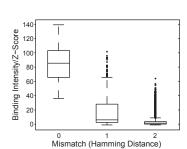


NFIL3 (73 nM)



ATTACGTAAT

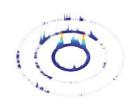


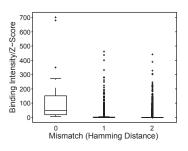


XBP1 (8 nM)



ATGACGTGGC





ATGACGCAAT

ATF3•CEBPA (13 nM)

ATF3•CEBPG (<1 nM)

ATF4•CEBPA (<1 nM)

ATF4•CEBPG (<1 nM)

Heterodimer

(PPI, Kd)

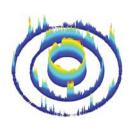




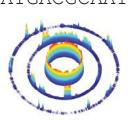
ATGACGCAAT



ATGACGCAAT



ATGACGCAAT



ATGACGCAAT

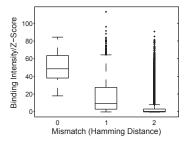


CTGATGCAAC

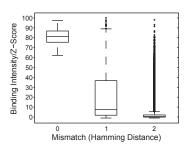


90-80-70-60-50-40-30-20-10-0-Binding Intensity/Z-Score

Mismatch (Hamming Distance)



45· 40· 35· 30· 25· 20· 15· 10· 5· Binding Intensity/Z-Score 0 1 2 Mismatch (Hamming Distance)



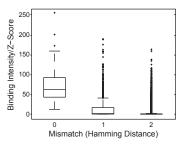
Binding Intensity/Z-Score 丄 0 1 2 Mismatch (Hamming Distance)

ATF5•CEBPE (28 nM)

ATF5•CEBPA (54 nM)







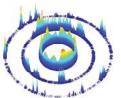
ATGACGCAAT

ATF5•CEBPG (<1 nM)

Heterodimer

(PPI, Kd)





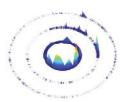
ATGACGTCAT

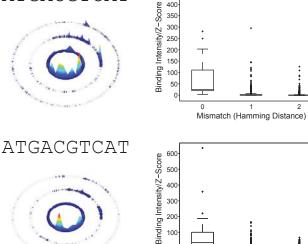


Binding Intensity/Z-Score 100 0 1 2 Mismatch (Hamming Distance)

ATF5•ATF6B (>5000 nM)







200

400

350

300 250

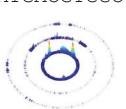
200 150

ATF5•BATF (187 nM)





ATGACGTGGC



120 Binding Intensity/Z-Score 100 Mismatch (Hamming Distance)

Mismatch (Hamming Distance)

ATF5•BATF2 (>5000 nM)

ATF5•BATF3

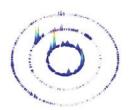
(385 nM)



E

E

ATGACGTGGC



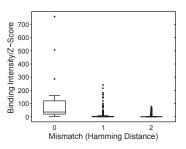
ATGACGTCAT



0 1 2 Mismatch (Hamming Distance)

ATF5•CREBZF (1541 nM)





ATGACGTCAT

ATF5•CREB3L1 (>5000 nM)

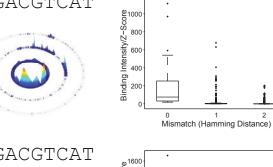
Heterodimer

(PPI, Kd)





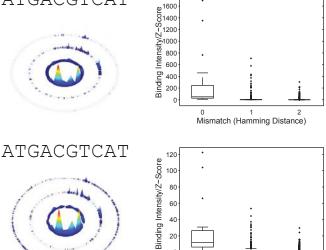
ATGACGTCAT



ATF5•CREB3L3 (>5000 nM)

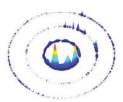




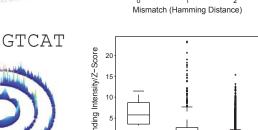


ATF5•FOS (>5000 nM)





ATGACGTCAT

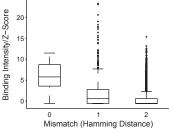


ATF5•JUN (>5000 nM)



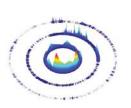


ATGACGTCAT

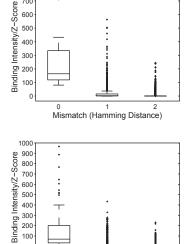


ATF5•JUNB (>5000 nM)





ATGACGTGGC

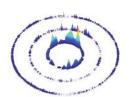


Mismatch (Hamming Distance)

BATF•ATF3 (17 nM)



E



BATF•CEBPA (10 nM)

Heterodimer

(PPI, Kd)



Ε



BATF•CEBPE (23 nM)



Ε



BATF•CEBPG (<1 nM)



C



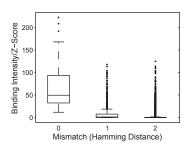
eu 250 OS-7 200 OS-7 200

BATF•CEBPG (<1 nM)



С





BATF•HLF (21 nM)



C



ATGACGTCAT

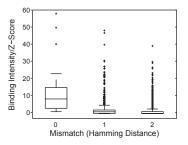
BATF•NFIL3 (291 nM)



C



ATGACGTCAT



Box plot for SEL rings

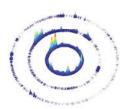
BATF2•ATF3 (429 nM)

Heterodimer

(PPI, Kd)



Ε



ATGACGTGGC

9 350 300 250 250 300 150 150 0 1 1 2 Mismatch (Hamming Distance)

BATF2•ATF4 (11 nM)



Ε

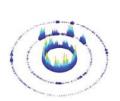


ATGACGTGGC

BATF2•JUN (<1 nM)



V



ATGAGTCAT

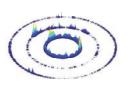
Binding Intensity/Z-Soore

Mismatch (Hamming Distance)

BATF2•JUN (<1 nM)



Ε



ATGACGTGGC

Binding Intensity/Z-Score

0 1 2 Mismatch (Hamming Distance)

BATF3•ATF3 (5 nM)



Ε

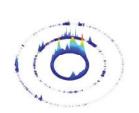


ATGACGTGGC

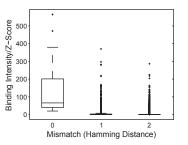
BATF3•ATF4 (4 nM)



Ε



ATGACGTGGC



Sequence Specificity & Energy Landscape (SEL)

Box plot for SEL rings

BATF3•CEBPA (5 nM)

BATF3•CEBPG

(2 nM)

Heterodimer

(PPI, Kd)

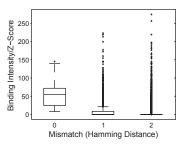




ATGACGCAAT

ATGACGCAAT



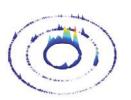


Binding Intensity/Z-Score 250 100 Mismatch (Hamming Distance)

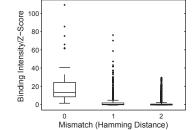
BATF3•NFIL3 (150 nM)



Ε



ATGACGTGGC

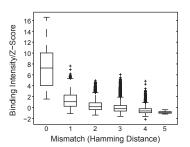


DDIT3•CEBPG (<1 nM)





ATTGCA

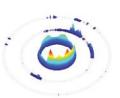


FOS•ATF2 (5 nM)





ATGACGTCAT



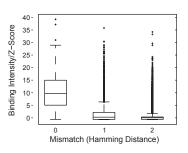
ATGAGTCAT



Binding Intensity/Z-Score 200 200 200 100 0 1 2 Mismatch (Hamming Distance)

FOS•ATF3 (185 nM)





ATGACGTCAT

FOS•ATF4 (4 nM)



C



e 600-GOS-Z/Z/500-JUDIUS UNITED TO STATE OF THE PROPERTY O

700

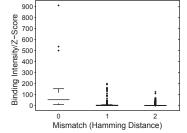
FOS•BATF (3593 nM)



C



ATGACGTCAT



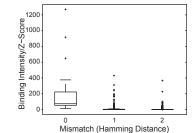
FOS•BATF2 (>5000 nM)



C



ATGACGTCAT



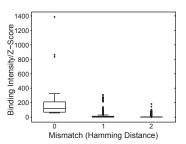
FOS•BATF3 (481nM)



C



ATGACGTCAT



FOS•CEBPE (239nM)

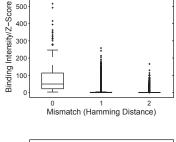


V



ATGAGCAAT

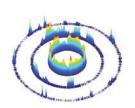
ATGACGCAAT

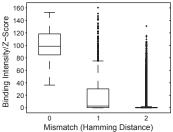


FOS•CEBPG (26nM)



C





Sequence Specificity & Energy Landscape (SEL)

Box plot for SEL rings

FOS•CREB3 (>5000 nM)

Heterodimer

(PPI, Kd)







120 Binding Intensity/Z-Score 100 80 0 1 2 Mismatch (Hamming Distance)

FOS•CREB3L3 (>5000 nM)



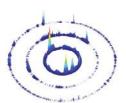
ATGACGTCAT



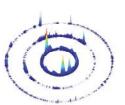
0 1 2 Mismatch (Hamming Distance)

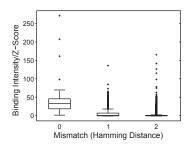
FOS•DBP (>5000 nM)





ATGACGTTAC



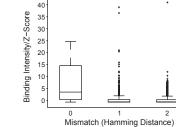


FOS•FOSL1 (<1 nM)





ATGAGTCAT



FOS•JUN

(<1 nM)





ATGAGTCAT

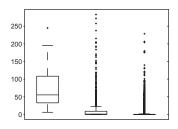


Binding Intensity/Z-Score 300 250 200 100 0 1 2 Mismatch (Hamming Distance)

FOS•MAFB (63 nM)







ATGAGTCAT

FOS•NFE2 (>5000 nM)

Heterodimer

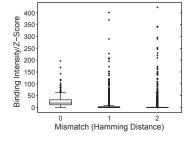
(PPI, Kd)



C



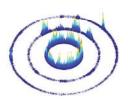
ATGAGTCAT



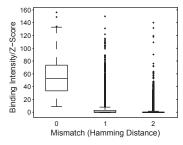
FOS•NFE2L1 (>5000 nM)



C



ATGAGTCAT



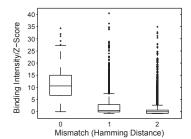
FOSL1•ATF3 (233 nM)



V



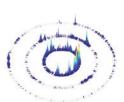
.11011010111



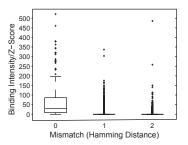
FOSL1•BATF3 (481 nM)



V



ATGAGTCAT



FOSL1•CEBPA (349 nM)



C



Binding Intensity/Z-Score

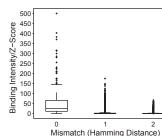
50 40

30

20 10

ATGACGCAAT

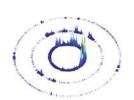
ATGAGCAAT



0 1 2 Mismatch (Hamming Distance)

1 2 3 4 5 6 7 8 9 10 11

V



FOSL1•CEBPE (266 nM)

Heterodimer

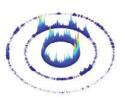
(PPI, Kd)

FOSL1•CEBPG (103 nM)

FOSL1•JUN

(<1 nM)





ATGAGTCAT





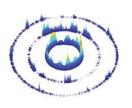
ATGAGTCAT



ATGACGCAT



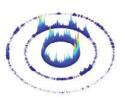
ATGACGCAAT



Binding Intensity/Z-Score

250

ATGAGTCAT



Binding Intensity/Z-Score 200 100

Mismatch (Hamming Distance)

Mismatch (Hamming Distance)

FOSL1•NFE2 (>5000 nM)





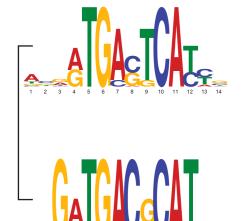
Binding Intensity/Z-Score 30 Mismatch (Hamming Distance)

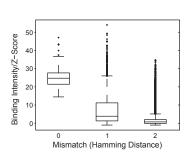
ATGAGTCAT

Binding Intensity/Z-Score 80 0 1 2 Mismatch (Hamming Distance)

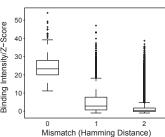
JUN•ATF3 (5 nM)

FOSL1•NFE2L1 (>5000 nM)





Binding Intensity/Z-Score 30 10



JUN•ATF3 (5 nM)

Sequence Specificity & Energy Landscape (SEL)

ATGACGCAAT

Box plot for SEL rings

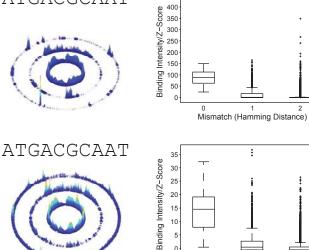
JUN•CEBPA (>5000 nM)

Heterodimer

(PPI, Kd)





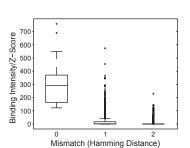


JUN•CEBPG (289 nM)





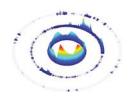
ATGACGTCAT



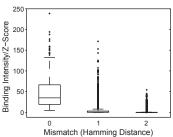
Mismatch (Hamming Distance)

JUNB•ATF2 (891nM)





ATGAGTCAT

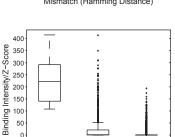


JUNB•ATF3 (8nM)





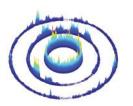
ATGACGTCAT



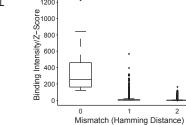
Mismatch (Hamming Distance)

JUNB•ATF3 (8nM)





ATGACGTCAT





JUNB•ATF4 (266 nM)



JUNB•BATF (<1 nM)

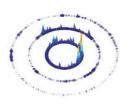
Heterodimer

(PPI, Kd)



C

ATGAGTCAT



450 9 400 9 350 1 300 1 50 1 150 1 150 1 100

JUNB•BATF2 (4 nM)



С



Binding Interview of the state of the state

JUNB•BATF2 (4 nM)



ATGACGTCAT



Budgud Distance)

JUNB•BATF3 (2 nM)



С



JUNB•BATF3 (2 nM)



C. E

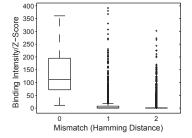
ATGACGTCAT



ATGACGCAAT

JUNB•CEBPA (>5000 nM)





JUNB•CEBPE (1697 nM)

Heterodimer

(PPI, Kd)



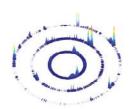




Binding Intensity/Z-Score 250 200 150 100 Mismatch (Hamming Distance)

JUNB•CEBPG (>5000 nM)





ATGACGCAAT

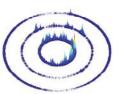
0 1 2 Mismatch (Hamming Distance)

JUNB•CREBZF (>5000 nM)





ATGAGTCAT



80 70 60 50 40 30 20 Binding Intensity/Z-Score Mismatch (Hamming Distance)

JUNB•DBP (>5000 nM)





Binding Intensity/Z-Score 50 40 30 20 0 1 2 Mismatch (Hamming Distance)

JUNB•FOS (2 nM)





0 1 2 Mismatch (Hamming Distance)

JUNB•FOSL1 (5 nM)

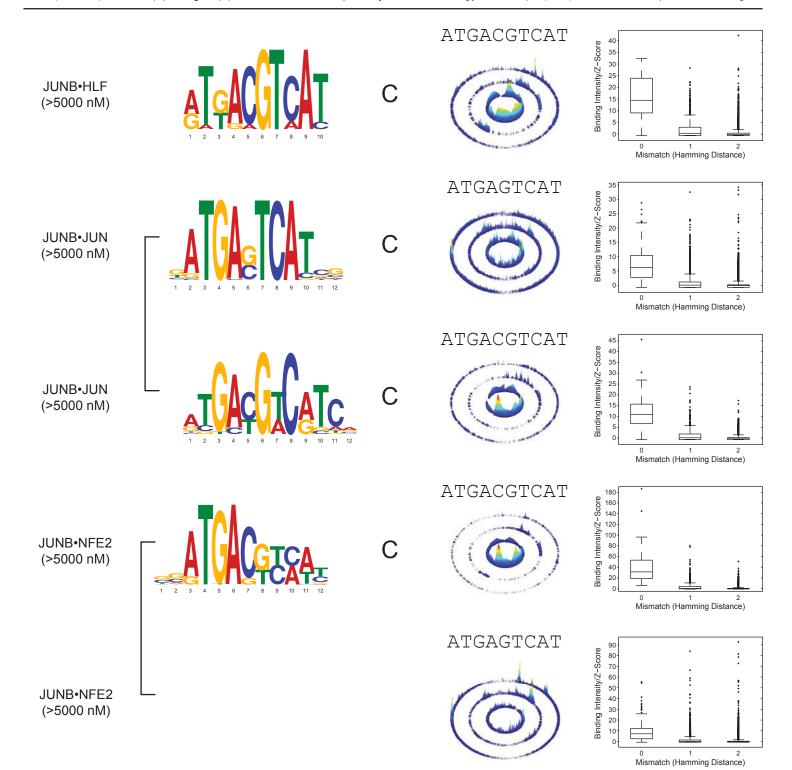




0 1 2 Mismatch (Hamming Distance) Heterodimer

(PPI, Kd)

Box plot for SEL rings



Sequence Specificity & Energy Landscape (SEL)

Box plot for SEL rings

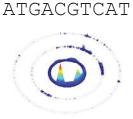
JUNB•NFE2L1 (>5000 nM)

(PPI, Kd)



(iii) emergent (E) based on homodimer specificity.

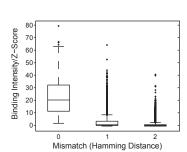
C



450 - 400 - 400 - 350 - 400 -

ATGAGTCAT





0 1 2 Mismatch (Hamming Distance)

JUNB•NFE2L1 (>5000 nM)

MAFB•ATF4 (193 nM)

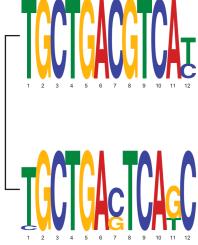


С

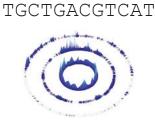


MAFB•ATF5 (>5000 nM)

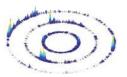
MAFB•ATF5 (>5000 nM)

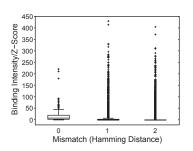


C



TGCTGAGTCAT





Heterodimer (PPI, Kd) MEME motif and classification as
(i) conjoined half-sites (C),
(ii) conjoined half-site with a variable spacer (V), or as
(iii) emergent (E) based on homodimer specificity.

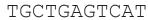
Sequence Specificity & Energy Landscape (SEL)

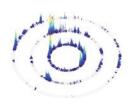
Box plot for SEL rings

MAFB•FOSL1 (152 nM)



C





NFE2•MAFG (1340 nM)



C



TGCTGAGTCAT

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NFE2L1•MAFG (<1 nM)



C



