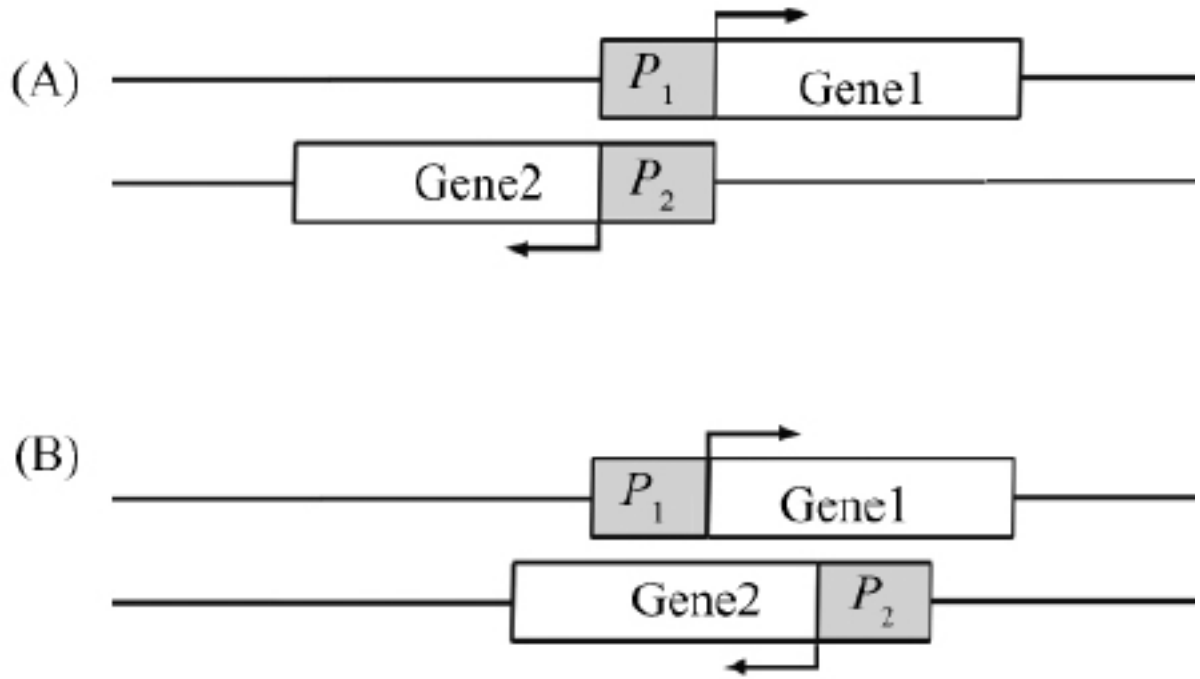
基态和进化

的

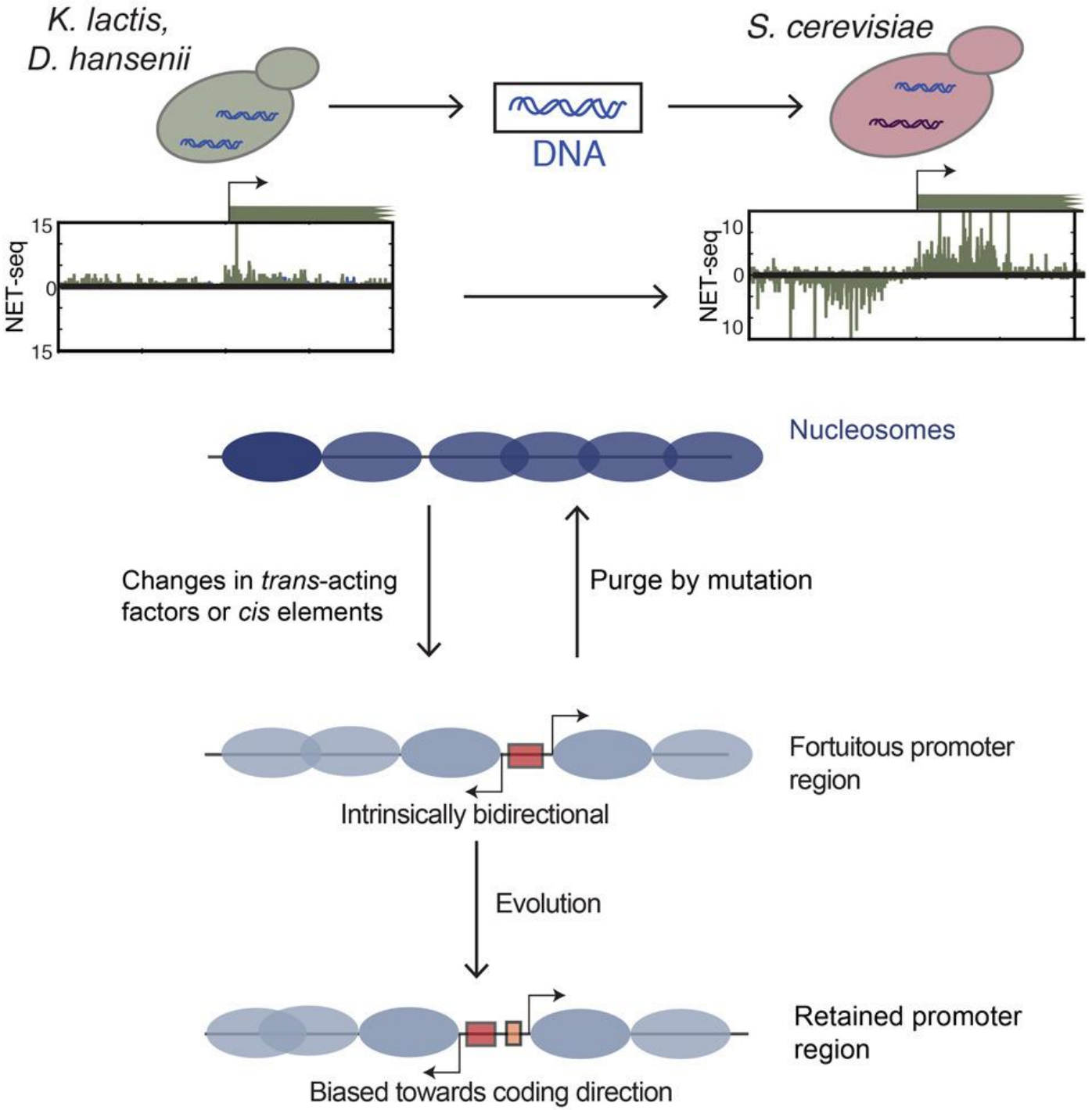
The Ground State and Evolution of Promoter Region Directionality

启动子区域方向性

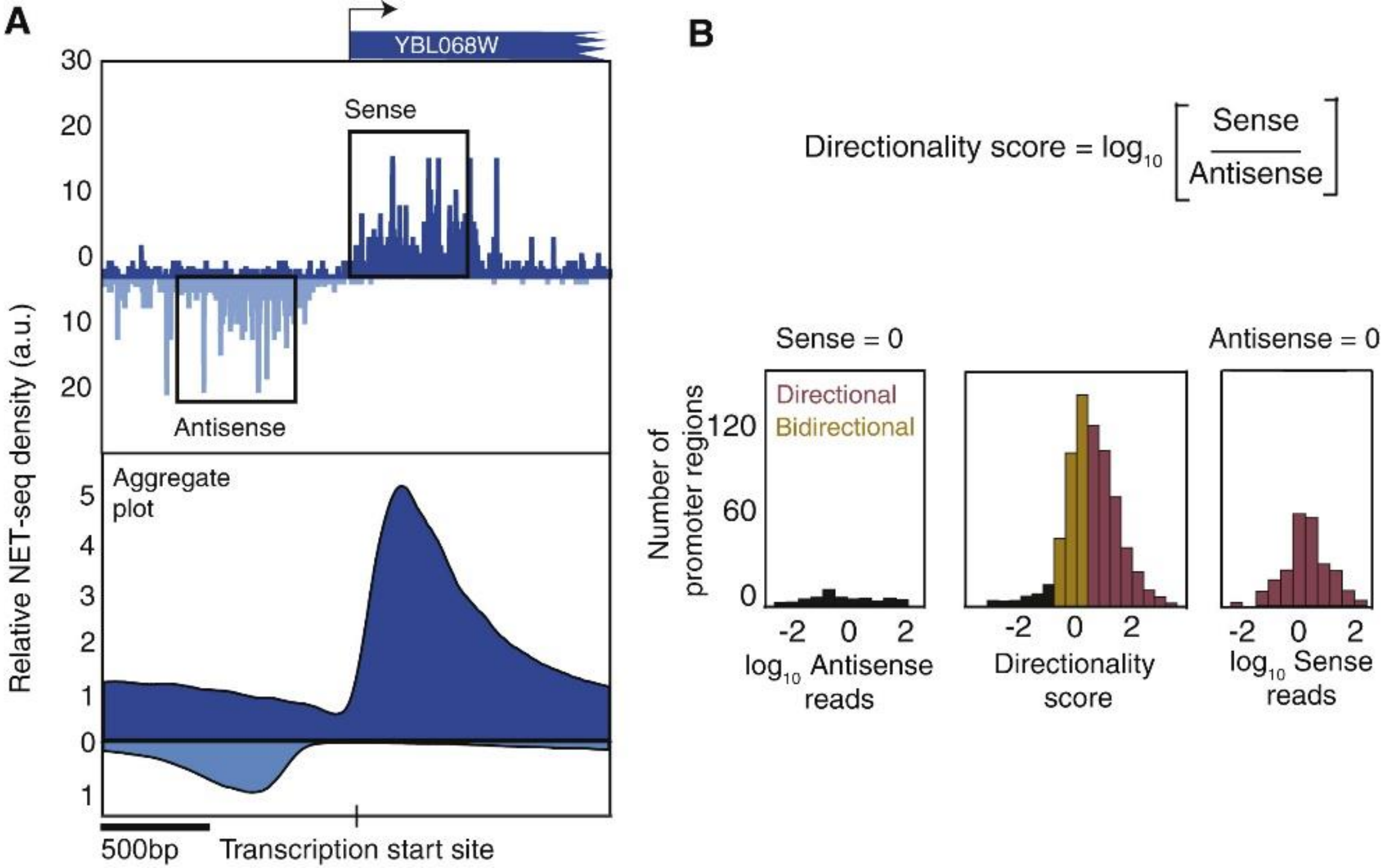
Introduction（1）



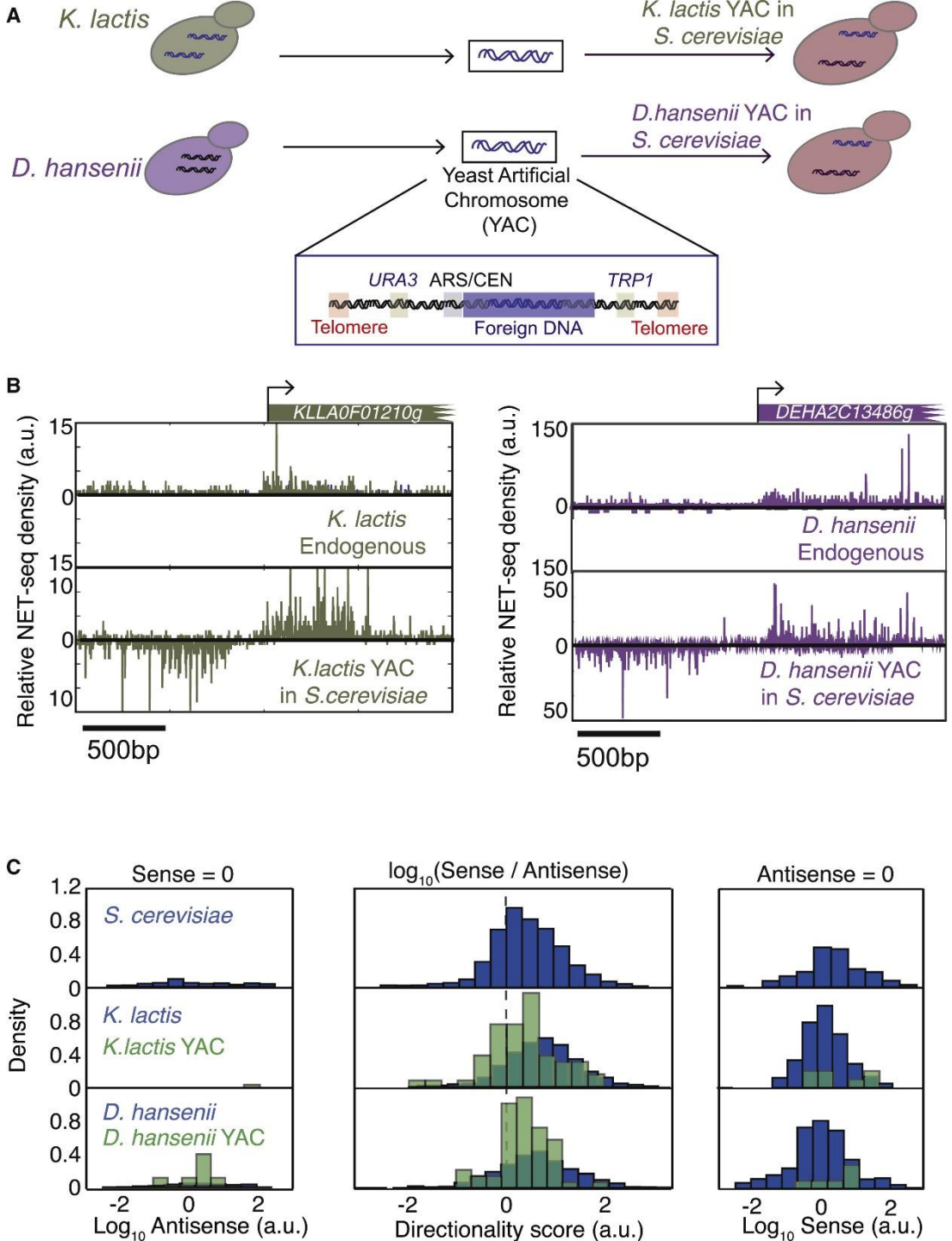
Introduction（2）



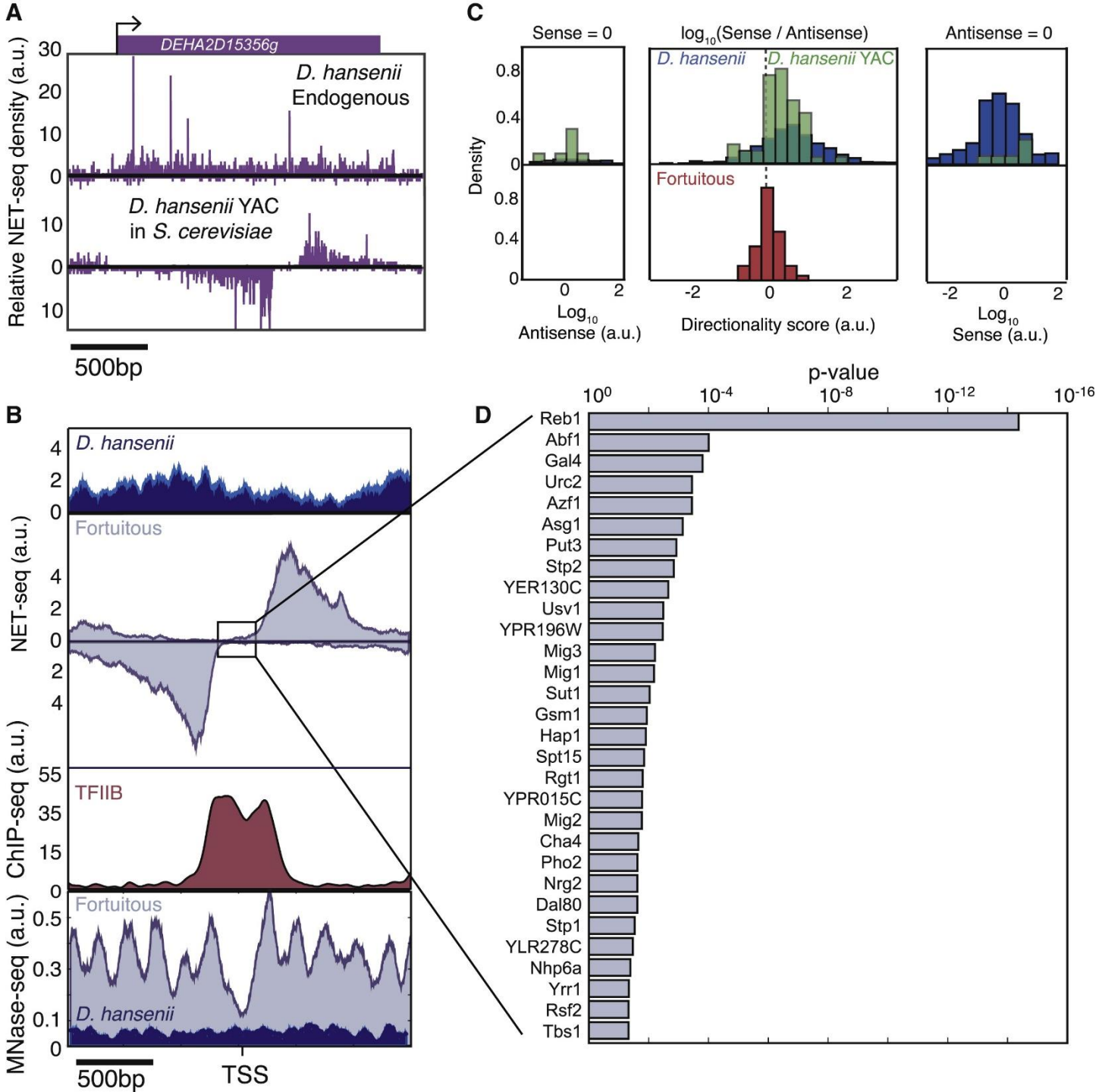
Transcription Is Biased toward the Coding Direction


A
YBL068W
Sense
Antisense
Relative NET-seq density (a.u.)
30
20
10
0
10
20
Aggregate plot
5
4
3
2
1
0
1
500bp
Transcription start site
B
Directionality score = log10 [Sense / Antisense]
Sense = 0
Antisense = 0
Number of promoter regions
120
60
0
Directional
Bidirectional
-2 0 2
log10 Antisense reads
Directionality score
log10 Sense reads

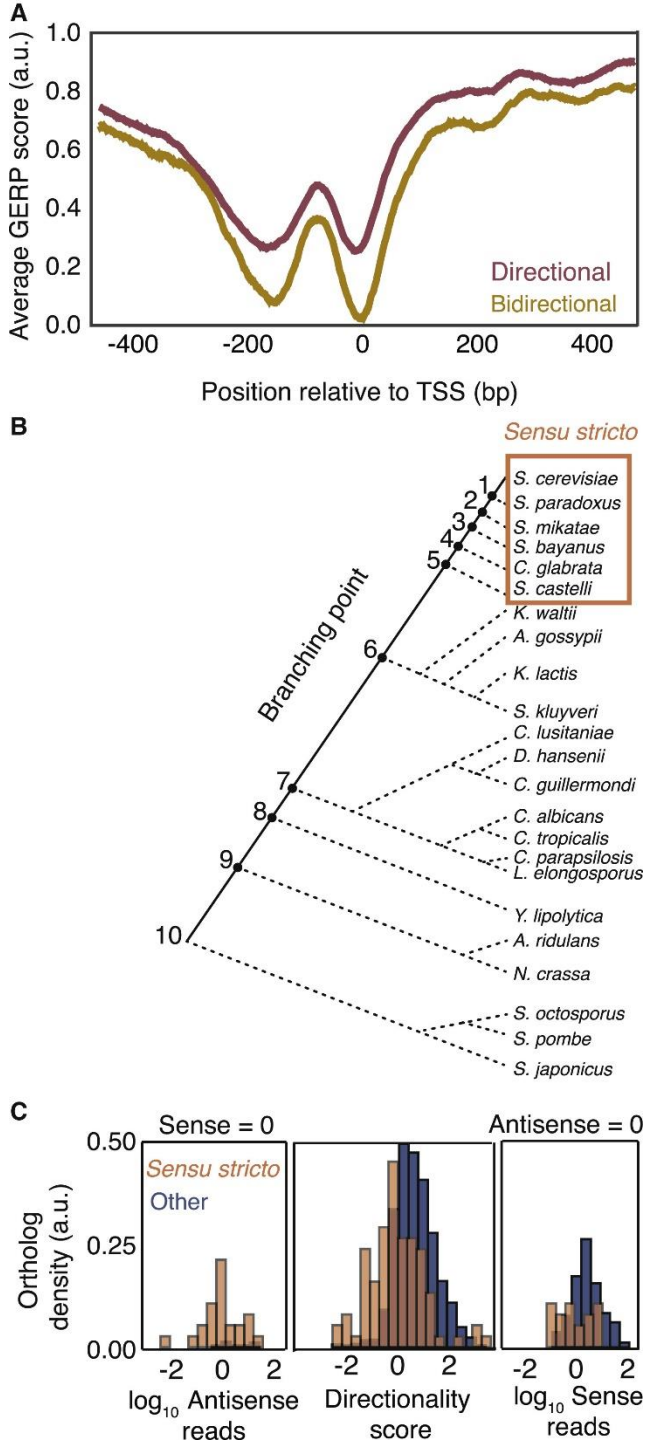
Directionality Loss in Foreign Environment


A
K. lactis
K. lactis YAC in S. cerevisiae
D. hansenii
D.hansenii YAC in S. cerevisiae
Yeast Artificial Chromosome (YAC)
URA3
ARS/CEN
TRP1
Telomere
Foreign DNA
Telomere
B
KLLA0F01210g
Relative NET-seq density (a.u.)
15
0
15
10
0
10
K. lactis Endogenous
K.lactis YAC in S.cerevisiae
500bp
DEHA2C13486g
150
0
150
50
0
50
D. hansenii Endogenous
D. hansenii YAC in S. cerevisiae
500bp
C
Sense = 0
log10(Sense / Antisense)
Antisense = 0
Density
1.2
0.8
0.4
0
S. cerevisiae
K. lactis
K.lactis YAC
D. hansenii
D. hansenii YAC
-2
0
2
Log10 Antisense (a.u.)
Directionality score (a.u.)
Log10 Sense (a.u.)

Fortuitous Promoter Regions Generate Equal Bidirectional Transcription


A
DEHA2D15356g
D. hansenii
Endogenous
D. hansenii YAC
in S. cerevisiae
Relative NET-seq density (a.u.)
500bp
B
D. hansenii
Fortuitous
NET-seq (a.u.)
TFIIB
ChIP-seq (a.u.)
MNase-seq (a.u.)
500bp
TSS
C
Sense = 0
log10(Sense / Antisense)
Antisense = 0
D. hansenii
D. hansenii YAC
Fortuitous
Density
Log10 Antisense (a.u.)
Directionality score (a.u.)
Log10 Sense (a.u.)
D
p-value
Reb1
Abf1
Gal4
Urc2
Azf1
Asg1
Put3
Stp2
YER130C
Usv1
YPR196W
Mig3
Mig1
Sut1
Gsm1
Hap1
Spt15
Rgt1
YPR015C
Mig2
Cha4
Pho2
Nrg2
Dal80
Stp1
YLR278C
Nhp6a
Yrr1
Rsf2
Tbs1

Newly Evolved Promoter Regions Are Less Directional Than Are More Evolved Promoter Regions


A
Average GERP score (a.u.)
1.0
0.8
0.6
0.4
0.2
0.0
-400
-200
0
200
400
Position relative to TSS (bp)
Directional
Bidirectional
B
Sensu stricto
Branching point
1
2
3
4
5
6
7
8
9
10
S. cerevisiae
S. paradoxus
S. mikatae
S. bayanus
C. glabrata
S. castelli
K. waltii
A. gossypii
K. lactis
S. kluyveri
C. lusitaniae
D. hansenii
C. guillermondi
C. albicans
C. tropicalis
C. parapsilosis
L. elongosporus
Y. lipolytica
A. ridulans
N. crassa
S. octosporus
S. pombe
S. japonicus
C
Sense = 0
Antisense = 0
Sensu stricto
Other
Ortholog density (a.u.)
0.50
0.25
0.00
-2
0
2
log10 Antisense reads
Directionality score
log10 Sense reads

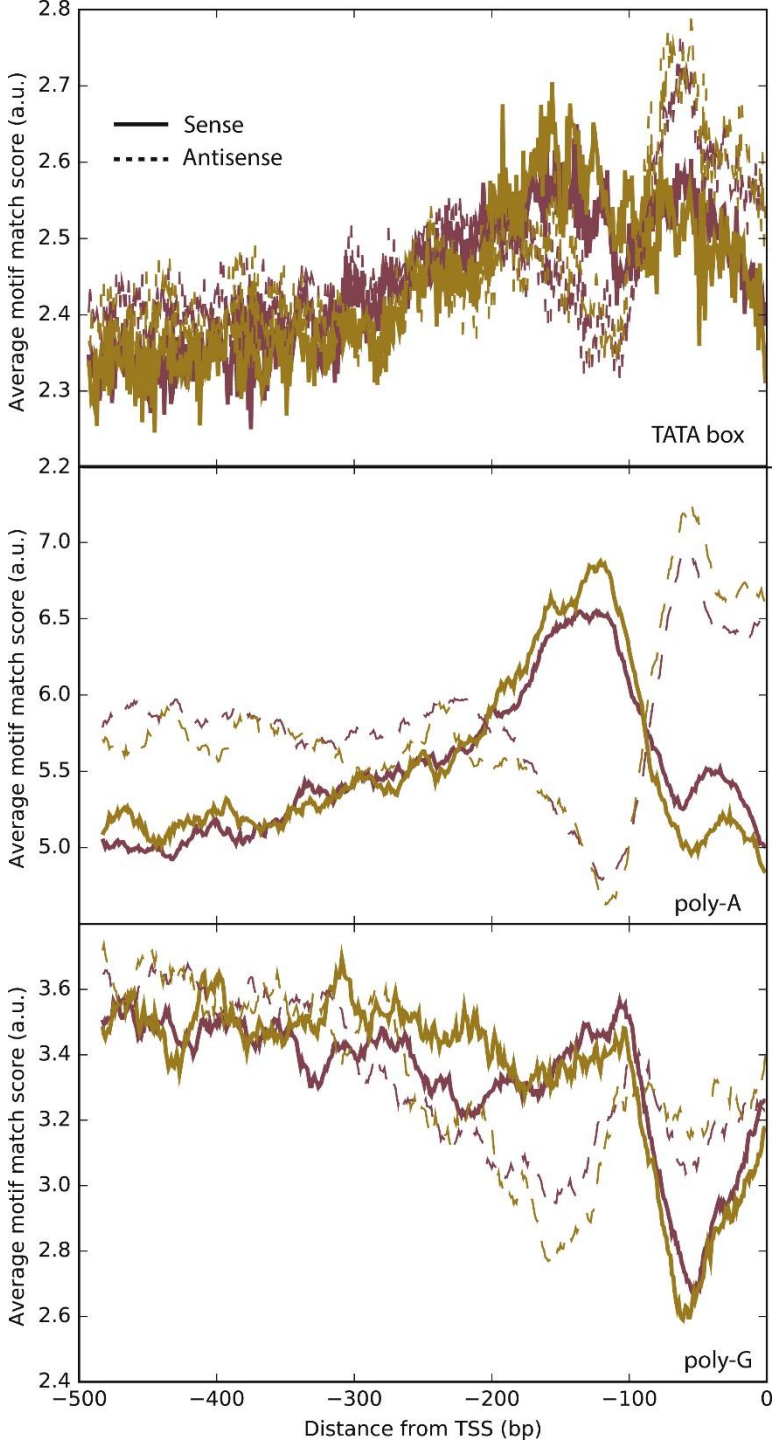
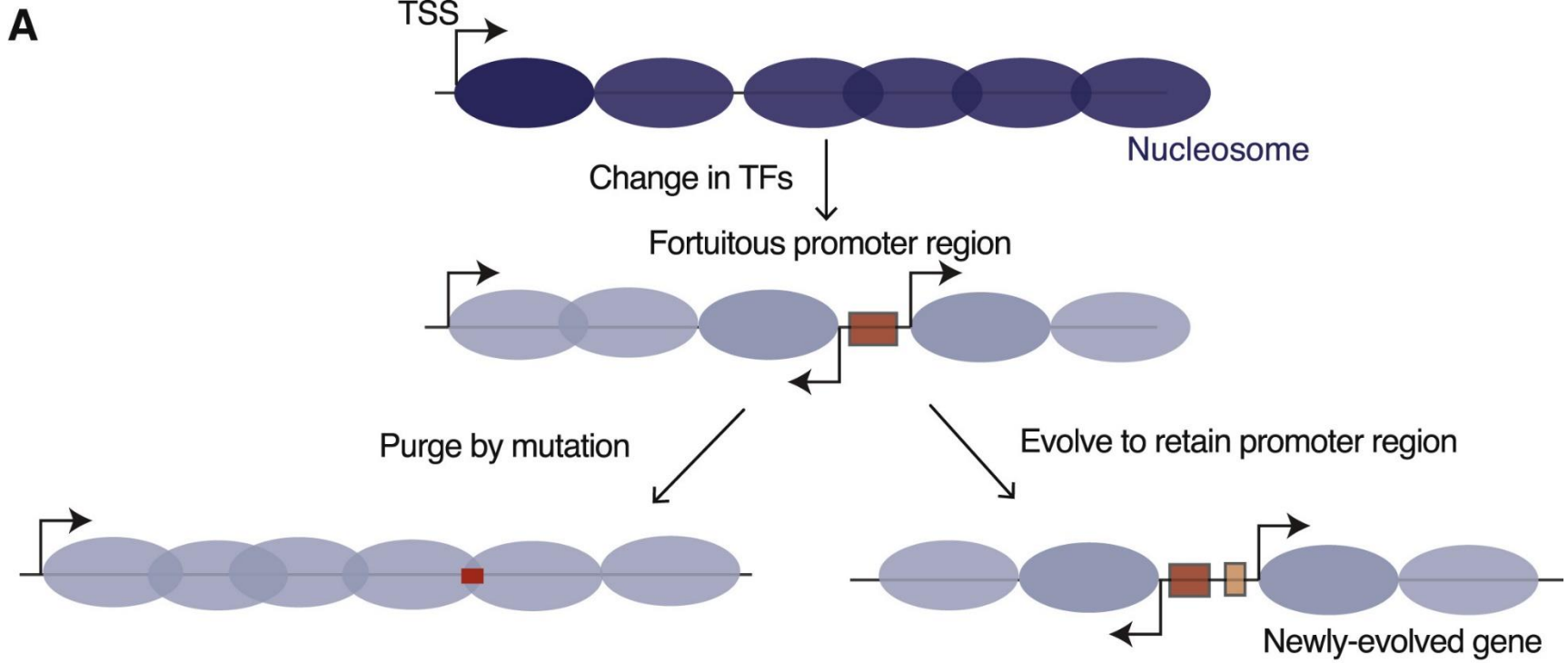


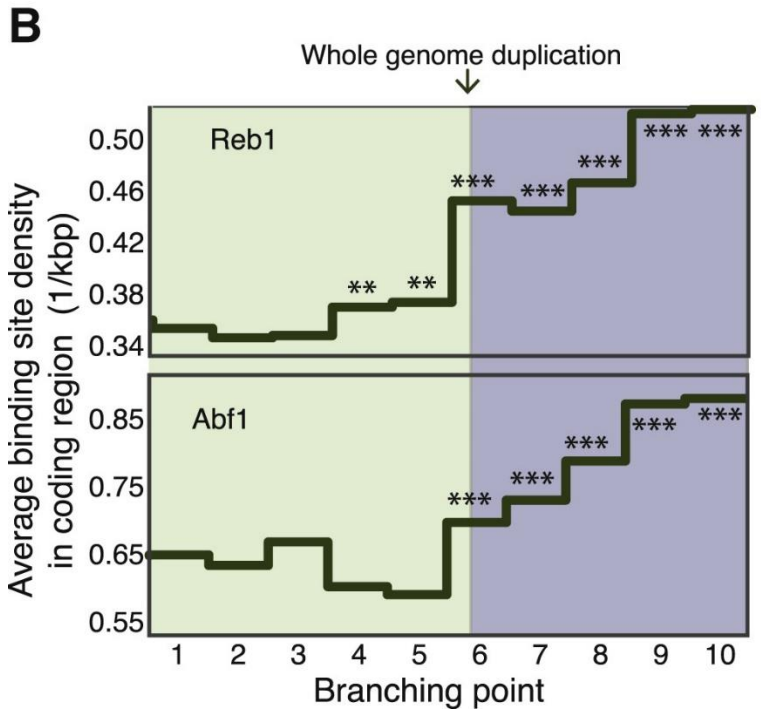
Table S2. Transcription factor binding motifs that have discriminative enrichment between directional and bidirectional promoter regions, Related to Figure 4

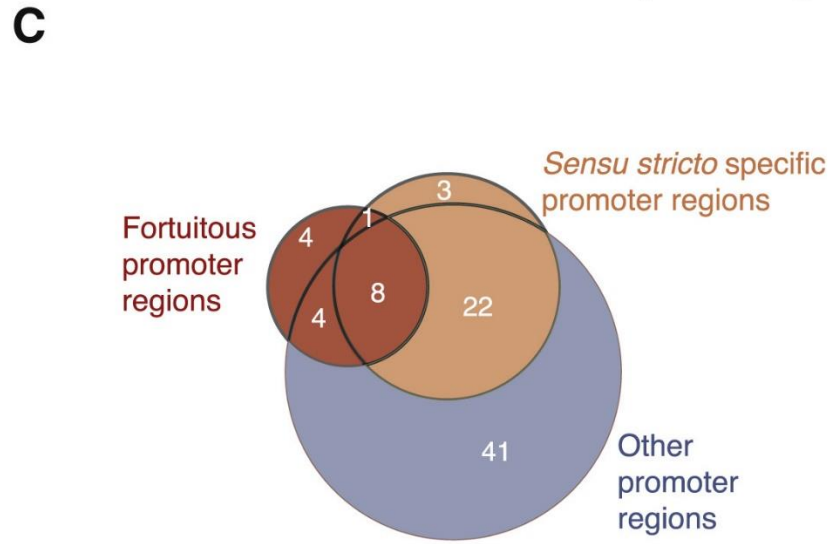
Transcription factor binding motifs that have discriminative enrichment between directional and bidirectional promoter regions. Mean log-ratio shows the average 10-based logarithm of maximum motif match scores differences between directional and bidirectional promoter regions. P values are obtained by the KS-test over the distributions of maximum motif match scores for both directional and bidirectional promoters.

	Mean log-ratio (directional/bidirectio	p-value
Cha4p_antisense	0.006339325	0.00390565
Hmra2p_sense	0.003912528	0.016470208
Mig1p_antisense	0.002225692	0.032306966
Mot3p_sense	0.003873016	0.03020083
Nhp6bp_antisense	0.002301217	0.039360207
Put3p_sense	0.002421579	0.017165191
Stp1p_antisense	0.003366996	0.009089037
Tbs1p_antisense	0.003779998	0.009791794
YKL222C_antisens	0.003439413	0.023826109
Yap1p_sense	0.00329624	0.02177999
Yrm1p_antisense	0.003972326	0.046828099
Yrr1p_sense	0.003315879	0.049660209

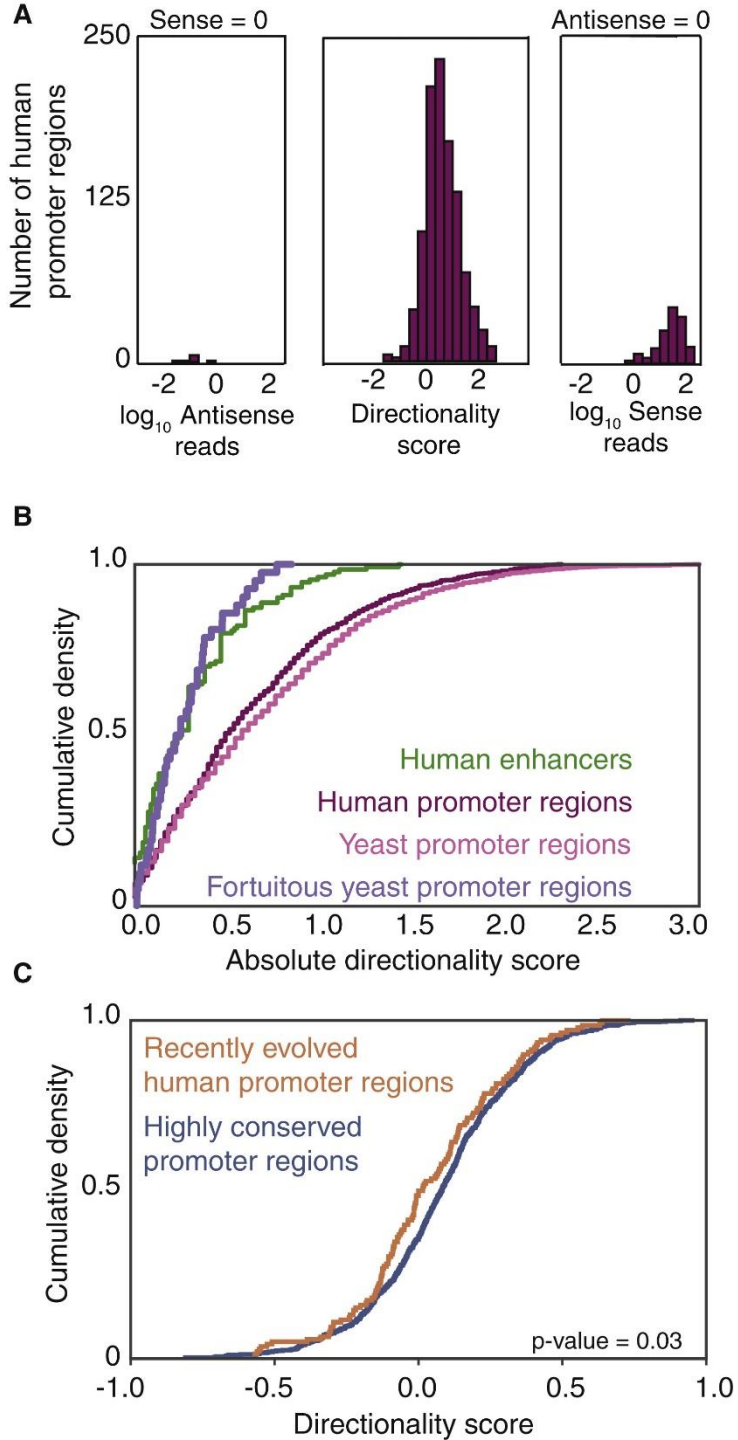
Evolutionary Resolution of Fortuitous Promoter Regions


A
TSS
Nucleosome
Change in TFs
Fortuitous promoter region
Purge by mutation
Evolve to retain promoter region
Newly-evolved gene


B
Whole genome duplication
Reb1
Abf1
Average binding site density in coding region (1/kbp)
0.50
0.46
0.42
0.38
0.34
0.85
0.75
0.65
0.55
1 2 3 4 5 6 7 8 9 10
Branching point


C
Sensu stricto specific promoter regions
Fortuitous promoter regions
Other promoter regions
3
1
4
8
22
4
41

Human Transcription Is Bidirectional at Newly Evolved Regulatory Regions


A
Sense = 0
Antisense = 0
250
125
0
Number of human promoter regions
-2 0 2
log10 Antisense reads
-2 0 2
Directionality score
-2 0 2
log10 Sense reads
B
1.0
0.5
0
Cumulative density
Human enhancers
Human promoter regions
Yeast promoter regions
Fortuitous yeast promoter regions
0.0 0.5 1.0 1.5 2.0 2.5 3.0
Absolute directionality score
C
1.0
0.5
0
Cumulative density
Recently evolved human promoter regions
Highly conserved promoter regions
p-value = 0.03
-1.0 -0.5 0.0 0.5 1.0
Directionality score

Conclusion

- 结论：
  - In brief, Promoter regions are intrinsically bidirectional and are shaped by evolution to bias transcription of coding transcripts, while suppressing noncoding antisense transcription.
- 优点：
  - 实验设计很巧妙，借助YAC质粒导入酿酒酵母查看其启动子的方向性
  - 设计了Directionality score用以评价启动子的方向性
- 缺点：
  - 对数据要求比较多，而且需要多个物种以构建进化层面的启动子方向性的改变
- 启发：
  - 从数据出发，广泛联系，精确推导，得出结论
- 改进
  - 优化Directionality score的定义，评价多个物种的进化性，寻找更普遍的规律