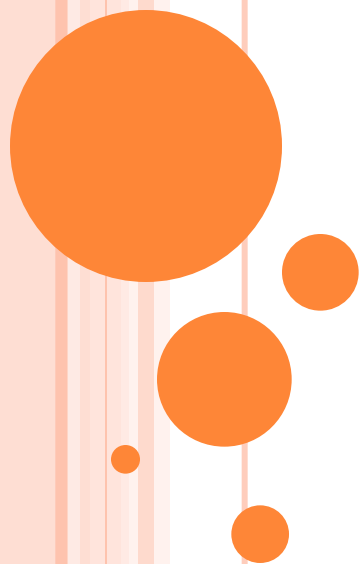


生物信息学学习汇报

北大二班 高珊

2010-06-12



二班学习交流总结

组号及报告人	题目	内容
G2 杨君娇	融合蛋白PE-NS site-eGFP-IPS-1的跨膜区域及三级结构预测	跨膜区及三级结构预测 (docking)
G3 贾均	From Pubmed To Gopubmed	PubMed; Gopubmed;SCI
G4 韦宝耶	The sequence, structure and function analysis of TIR1	全面：蛋白相互作用；亚细胞定位；信号肽分析；拟南芥数据库
G5 李钦	甲型H1N1流感病毒神经氨酸酶的药物结合位点分析	序列比对 (MUSCLE) 结构分析 (PyMOL)
G6 刘轶群	软件使用介绍	EndNote; Vector NTI
G7 秦伟	斑马鱼中Ppdpf蛋白的生物信息学分析	全面：ENSEMBL; 共线性和保守性分析; ZiFiT
G8 许楠	Protein Phosphorylation Sites Prediction	NetPhos; NetPhosK; NetPhosYeast; GPS

NMDA受体亚型的生物信息学分析

Class 2 Group 1:

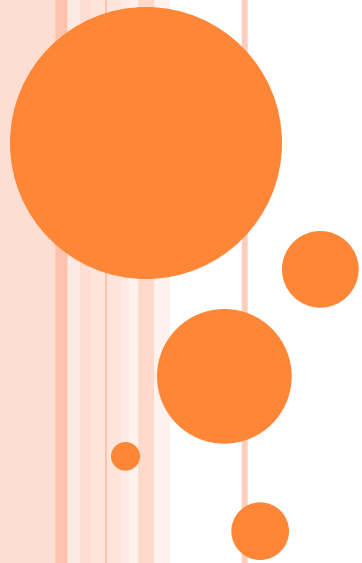
马祥

马寅燕

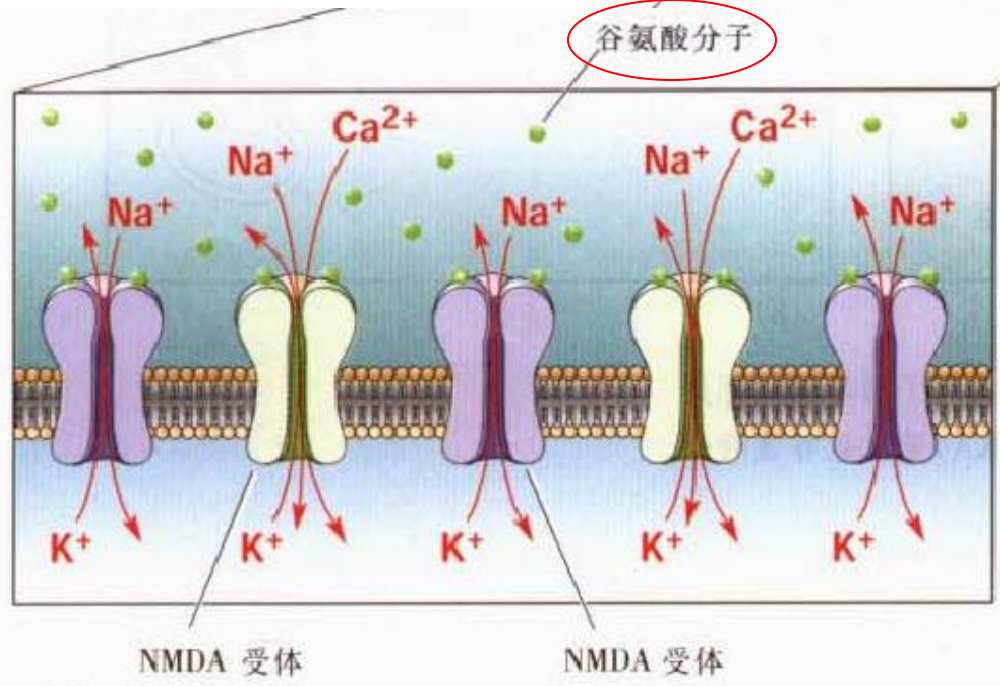
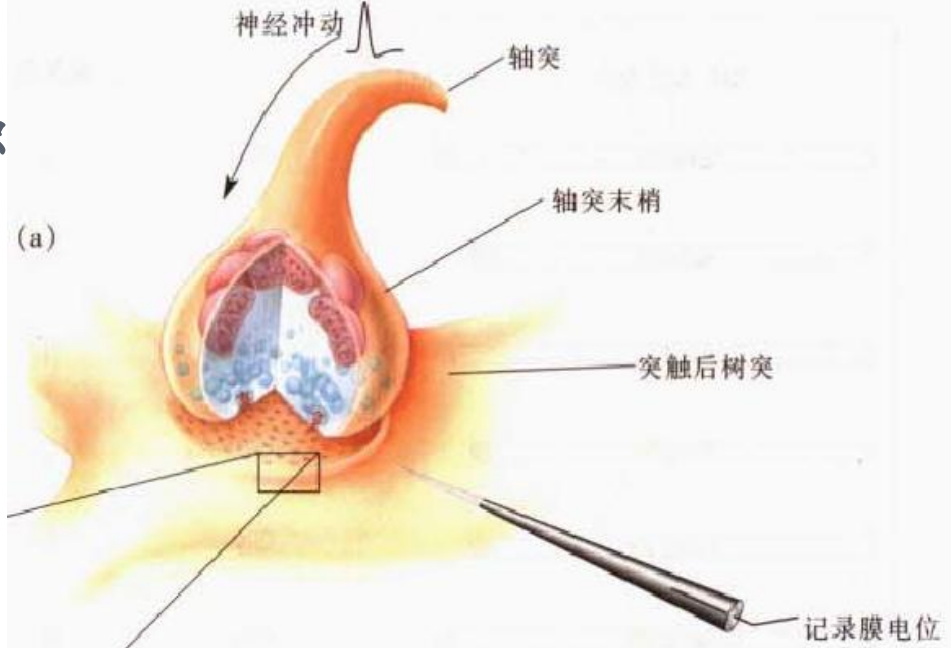
王云凤

高珊

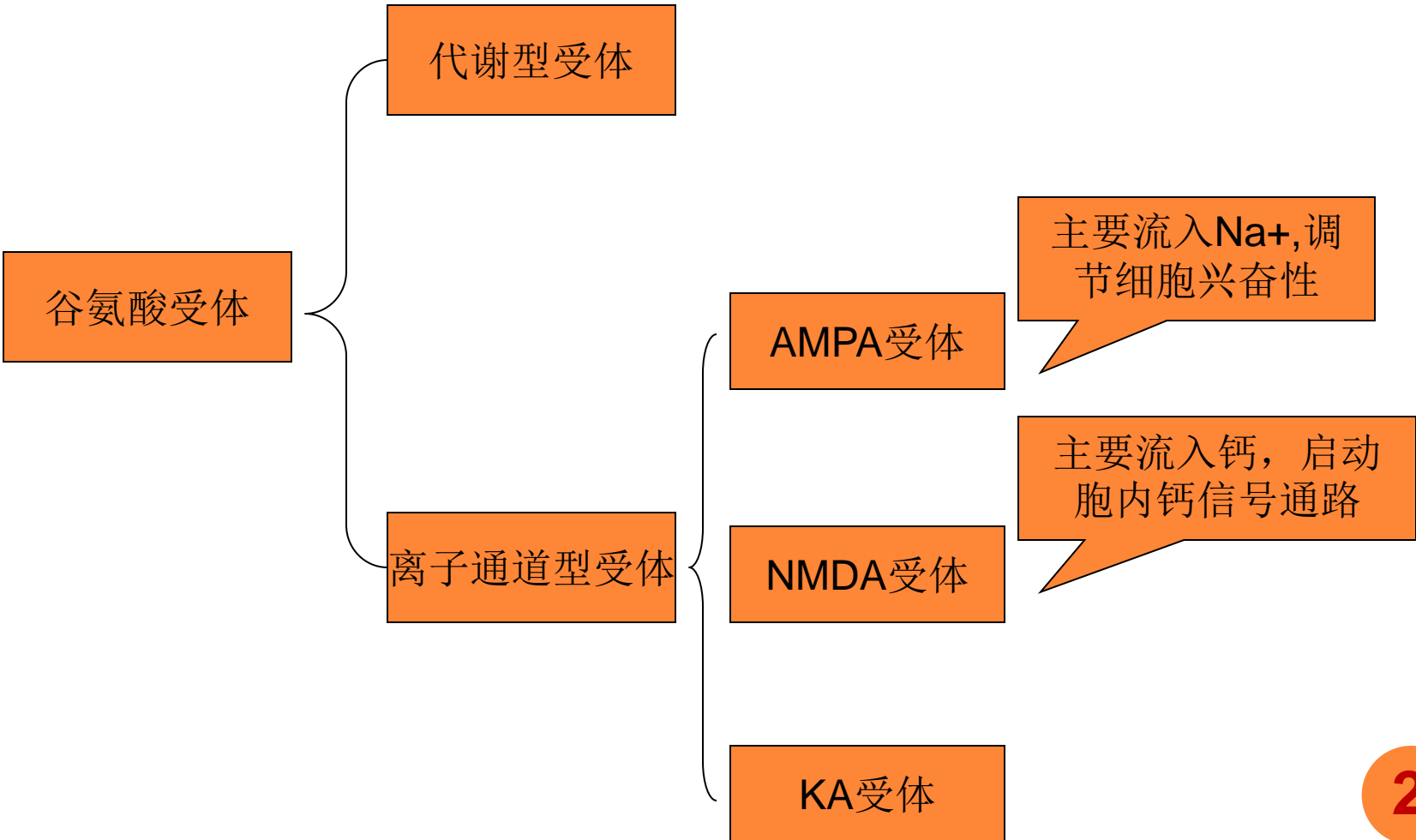
2010-06-12



神经系统的信息传递：突触

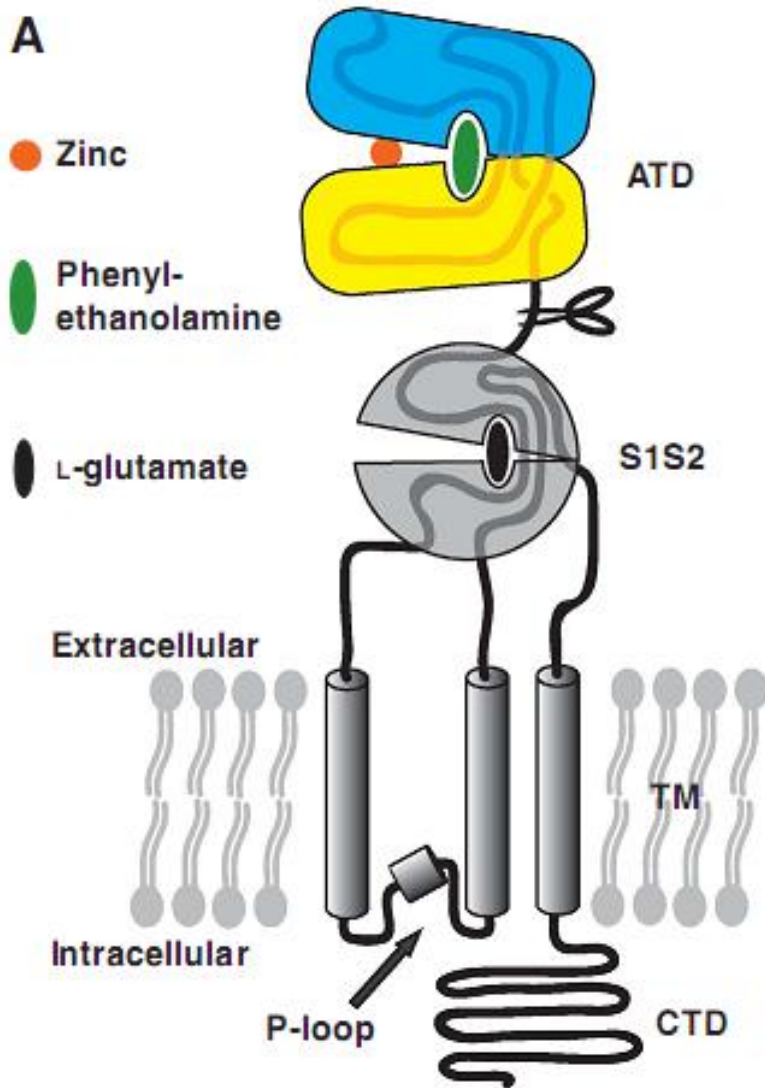


谷氨酸受体分类



NMDA受体介绍

- 离子型谷氨酸受体，激动剂为N-甲基-D-天冬氨酸 (N-methyl-D-aspartate, NMDA)
- 在LTP、LTD等学习和记忆形成相关的突触可塑性过程中发挥重要作用。
- 激活受谷氨酸配体结合和电压双重控制。
- **两个NR1与两个NR2亚基组成的异源四聚体**。胞外区N末端有变构调节区和配体结合区两个功能域，胞内的C末端可耦连下游信号通路。



NR1、NR2C、NR2D
的配体结合区结合共
激活物glycine，
NR2A、NR2B的配体
结合区结合递质
glutamate。

含有不同亚型NR2 亚基的NMDA受体生物学特性不同

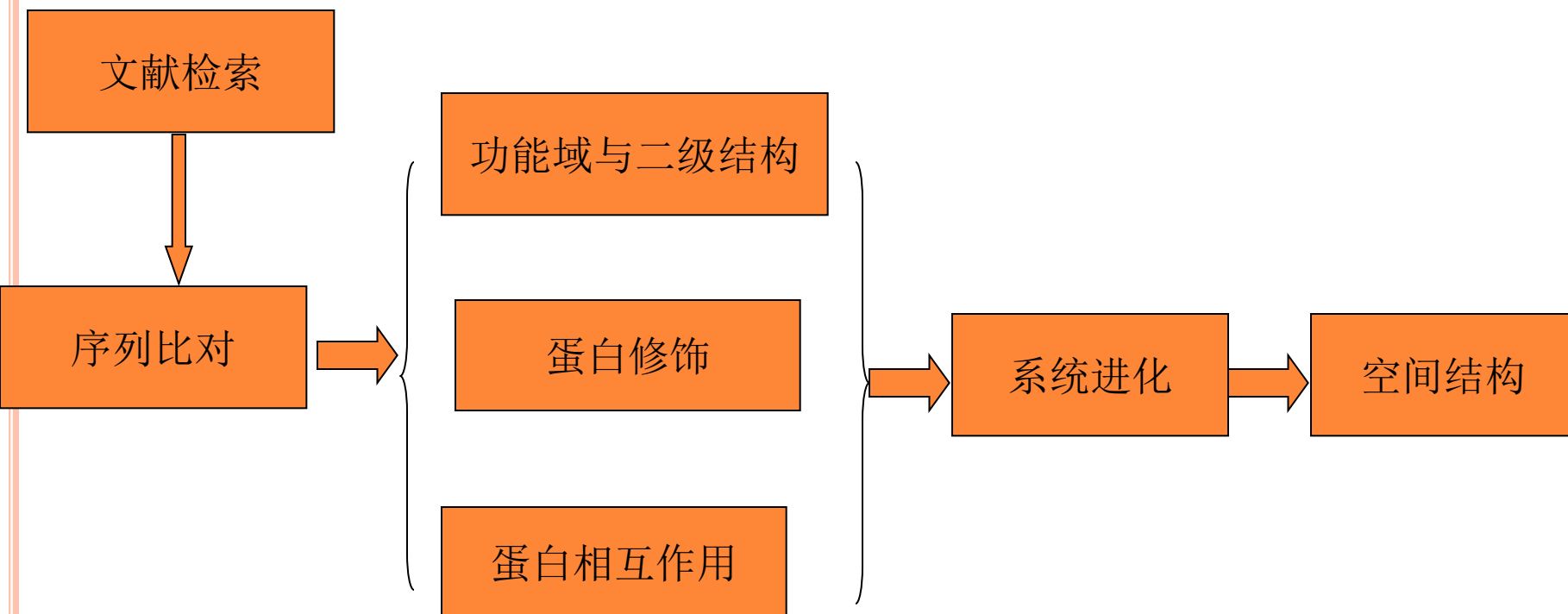
- **发育过程中的表达模式**：NR2A型逐渐替代突触区NR2B型受体。
- **突触成熟后受体的分布**：突触内多是含有NR2A的NMDA受体，突触外多为含NR2B的NMDA受体。
- **对LTP、LTD的影响**：选择性阻断NR2A型NMDA受体阻止了LTP的形成，而对LTD无影响；阻断NR2B型受体影响LTD的形成，而对LTP无影响。
- **脑缺血、中风等疾病**：突触外NR2B类型NMDA受体的激活与兴奋性毒损伤

我们关注的问题

- 同为NR2亚基，NR2A与NR2B表现出截然不同的生物学特性，其序列、结构等基本特征有何不同？
- NMDA受体与其离子型受体本质相适应的拓扑结构和磷酸化等修饰情况是怎样的？
- 两亚基与其他蛋白相互作用的情况如何？



生物信息学分析过程

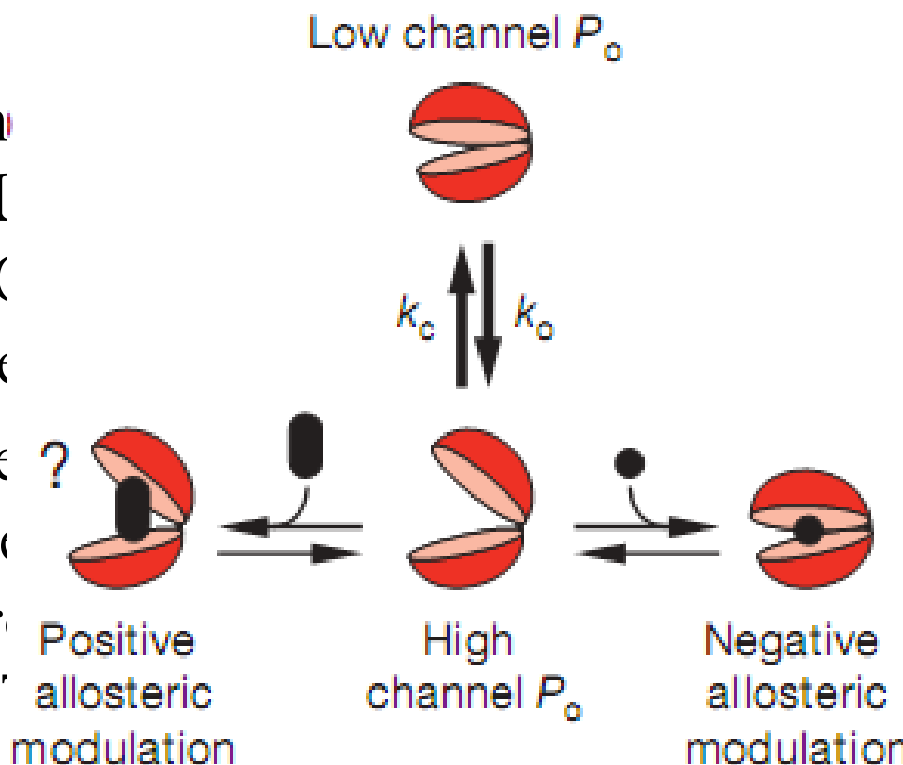


一、关于NR2亚基的文献报道 (PUBMED)

○ 通道动力学不同，如开放概率：

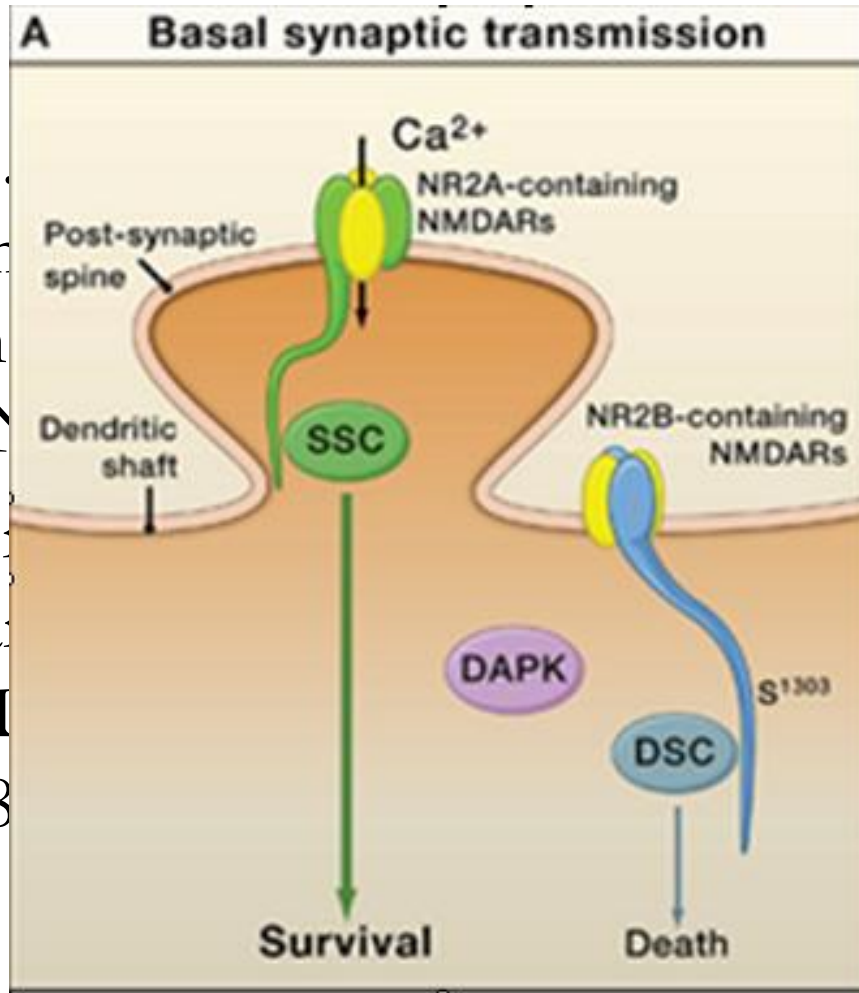
[1] Nanshen
Subtype-I
Channel (C
Neurosci

[2] Marc Gie
Mony. Mo
NMDA r



ond.
:
:
tia
of
. 2009,

○ 下游耦联的信号通路不同:



[1] Giles E.
Extrasynaptic
triggering
Nature M
[2] Rolf Sp
Importan
for NMD
279 - 28

a, Hilmar Bading.
otic NMDARs by
h pathways.
2.
a Amico et al.
of NR2 subunits
Cell. 1998, 92:

By Henry GS et al, 2010

二、序列比对与功能片段分析

- 序列比对:

Needle

- 跨膜区预测:

TMAP HMMTOP SOUSI TopPred TMHMM
ProtParam

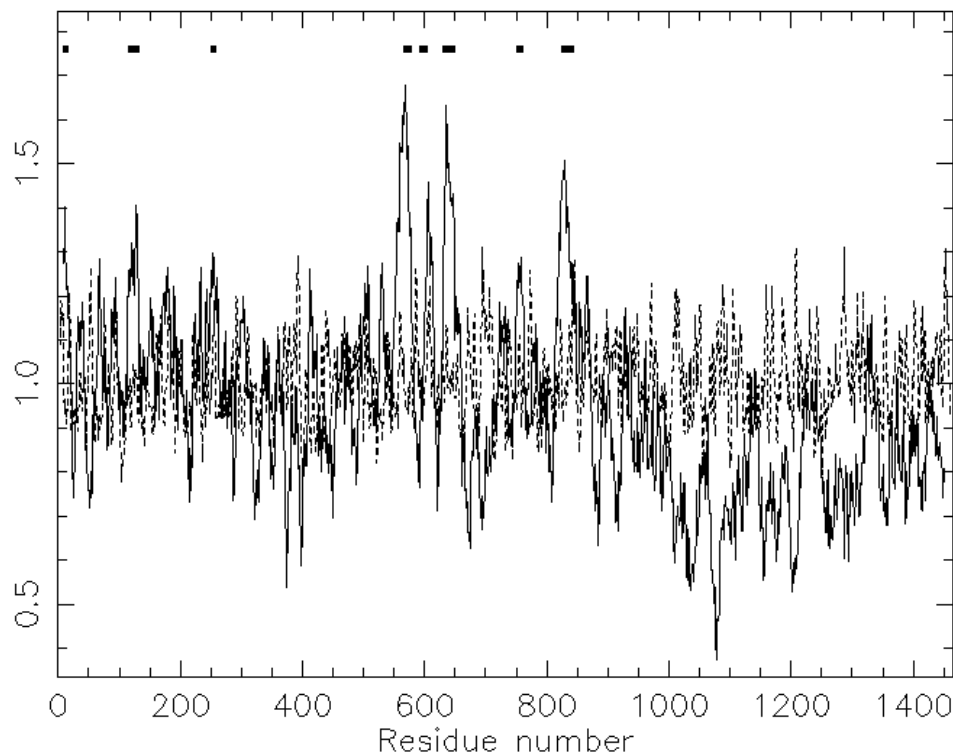
- 二级结构预测

GOR4 HNN SOPMA

跨膜区预测

TMAP

NR2A Tmap



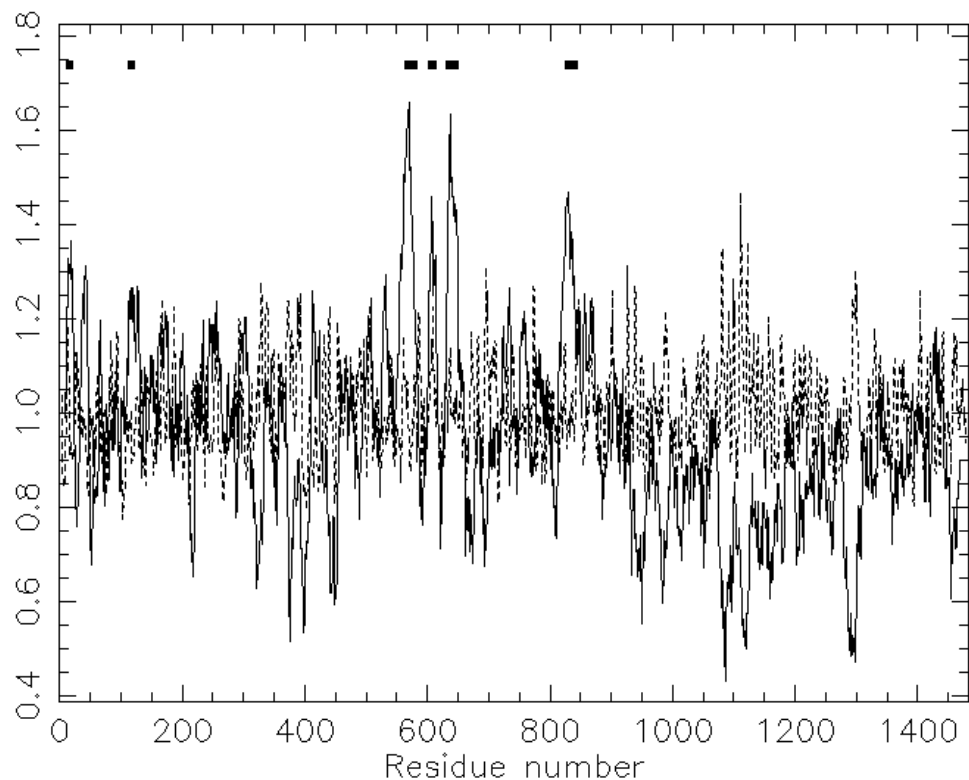
```
#####  
# Program: tmap  
# Rundate: Thu 3 Jun 2010 13:10:36  
# Commandline: tmap  
# -auto  
# -graph png  
# -sequences 338891  
# -goutfile 338962  
# -outfile 338963  
# Report_format: seqtable  
# Report_file: 338963  
#####  
#=====  
#  
# Sequence: Consensus from: 1 to: 1464  
# HitCount: 8  
#=====  
Start End TransMem Sequence  
4 20 1 LGYWTLLVLPALLVWRD  
111 136 2 QMLDFISSQTFIPILGIHGGASMIMA  
246 262 3 LGLTGYDFWIVPSLVS  
561 581 4 MFVMLLIVSAIAVFFVFEYFSP  
587 607 5 NLAKGKAPHGPSFTIGKAIWL  
626 653 6 TSKIMVSVWAFFAVIFLASYTANLAAFM  
746 765 7 KLVTIGSGYIFASTGYGIAL  
821 847 8 FYMLAAAMALSITFIWEHLFYWKLRF  
..
```

跨膜区预测

TMAP

NR2B

Tmap



```
#####
```

```
# Program: tmap
# Rundate: Thu 3 Jun 2010 13:11:20
# Commandline: tmap
# -auto
# -graph png
# -sequences 338893
# -goutfile 338964
# -outfile 338965
# Report_format: seqtable
# Report_file: 338965
#####
#
# Sequence: Consensus      from: 1   to: 1482
# HitCount: 6
```

```
#####
```

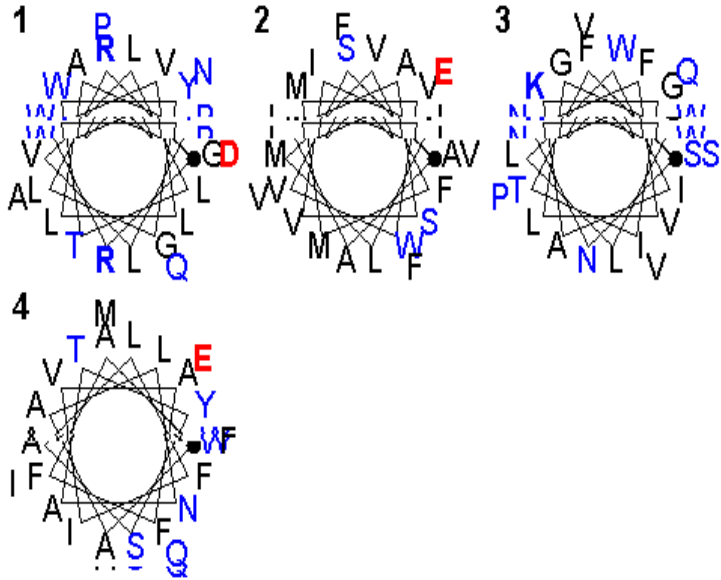
Start	End	TransMem	Sequence
8	25	1	CSPKF W LVLAVLAVSGSK
109	126	2	AQILD F ISAQTLTPILGI
559	587	3	WVM M FV L LIVS A VAVFVFEYFSPVGYNR
598	618	4	PSFTIGKAI W LLWGLVFNNSV
627	654	5	TSKIN V SV W AFFAVIFLASYTANLAAFM
822	848	6	FYMLGAAMALSLITTFICEHLFYWQFRH

跨膜区预测

SOSUI

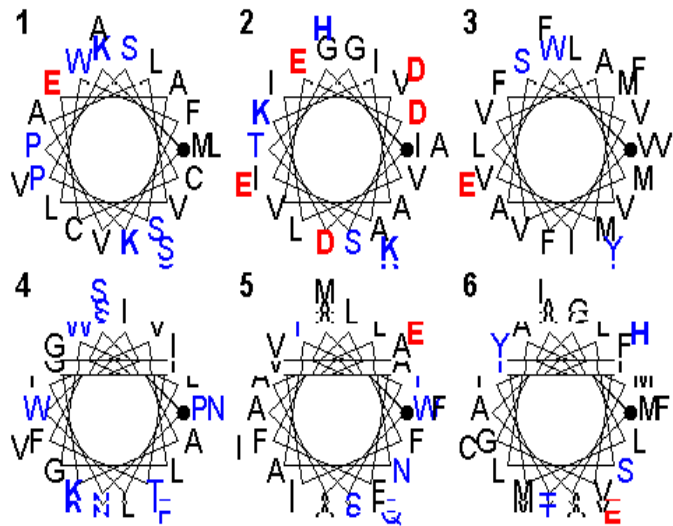
NR2A

No.	N terminal	transmembrane region	C terminal	type	length
1	2	GRLGYWTLVLPALLVWRDPAQN	24	SECONDARY	23
2	555	ASVWVMFVMLLIVSAIVFVFE	577	PRIMARY	23
3	598	SFTIGKAIWLLWGLVFNNVSPVQ	620	SECONDARY	23
4	634	WAFPAVIFLASYTANLAAPMIQE	656	SECONDARY	23



NR2B

No.	N terminal	transmembrane region	C terminal	type	length
1	1	MKPSAECCSPKFWLVLAFLAVS	22	SECONDARY	22
2	35	IGIAVILVGTSDVEVAIKDAHEKD	57	SECONDARY	23
3	558	VWVMFVMLLIVSAIVFVFEYF	580	PRIMARY	23
4	598	PSFTIGKAIWLLWGLVFNNVSP	619	SECONDARY	22
5	635	WAFPAVIFLASYTANLAAPMIQE	657	SECONDARY	23
6	818	MAGVPYMLGAAMALSLITFICEH	840	PRIMARY	23



跨膜区预测

TopPred - Topology prediction of membrane proteins

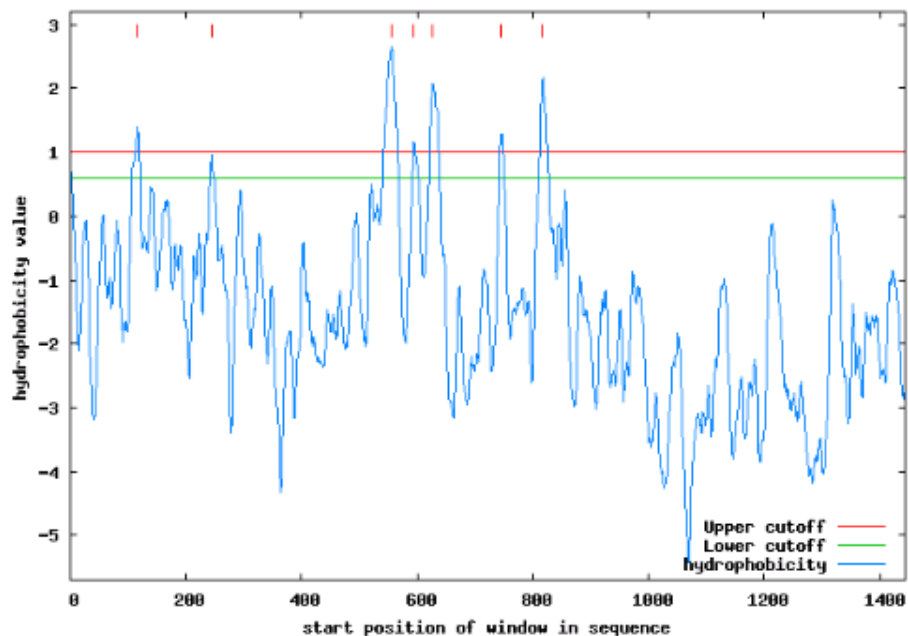
NR2A

Q00959	TMHMM2.0	outside	1	556	
Q00959	TMHMM2.0	TMhelix	557	579	1
Q00959	TMHMM2.0	inside	580	632	
Q00959	TMHMM2.0	TMhelix	633	655	2
Q00959	TMHMM2.0	outside	656	746	
Q00959	TMHMM2.0	TMhelix	747	765	3
Q00959	TMHMM2.0	inside	766	817	
Q00959	TMHMM2.0	TMhelix	818	837	4
Q00959	TMHMM2.0	outside	838	1464	

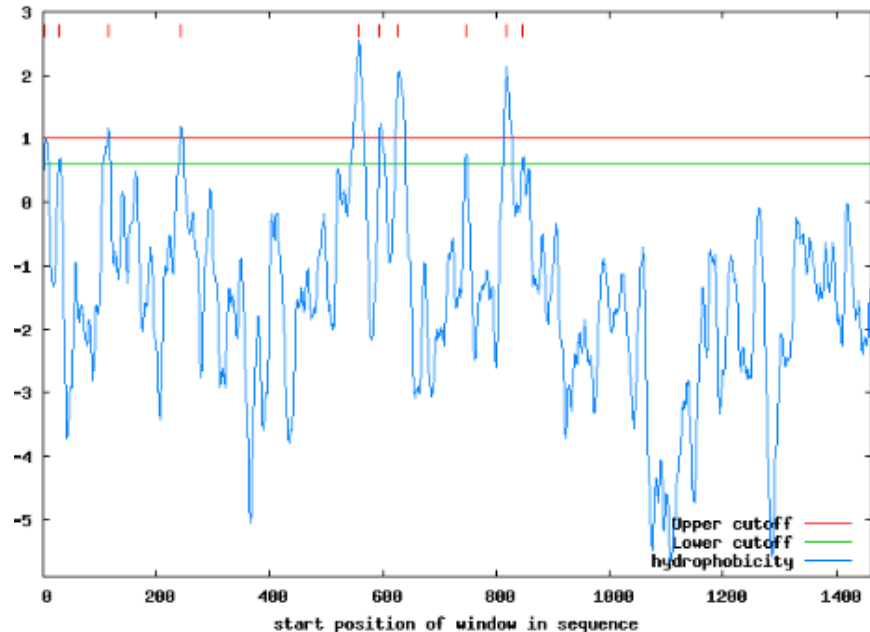
NR2B

Q00960	TMHMM2.0	outside	1	557	
Q00960	TMHMM2.0	TMhelix	558	580	1
Q00960	TMHMM2.0	inside	581	598	
Q00960	TMHMM2.0	TMhelix	599	621	2
Q00960	TMHMM2.0	outside	622	630	
Q00960	TMHMM2.0	TMhelix	631	653	3
Q00960	TMHMM2.0	inside	654	820	
Q00960	TMHMM2.0	TMhelix	821	843	4
Q00960	TMHMM2.0	outside	844	1482	

Q00959

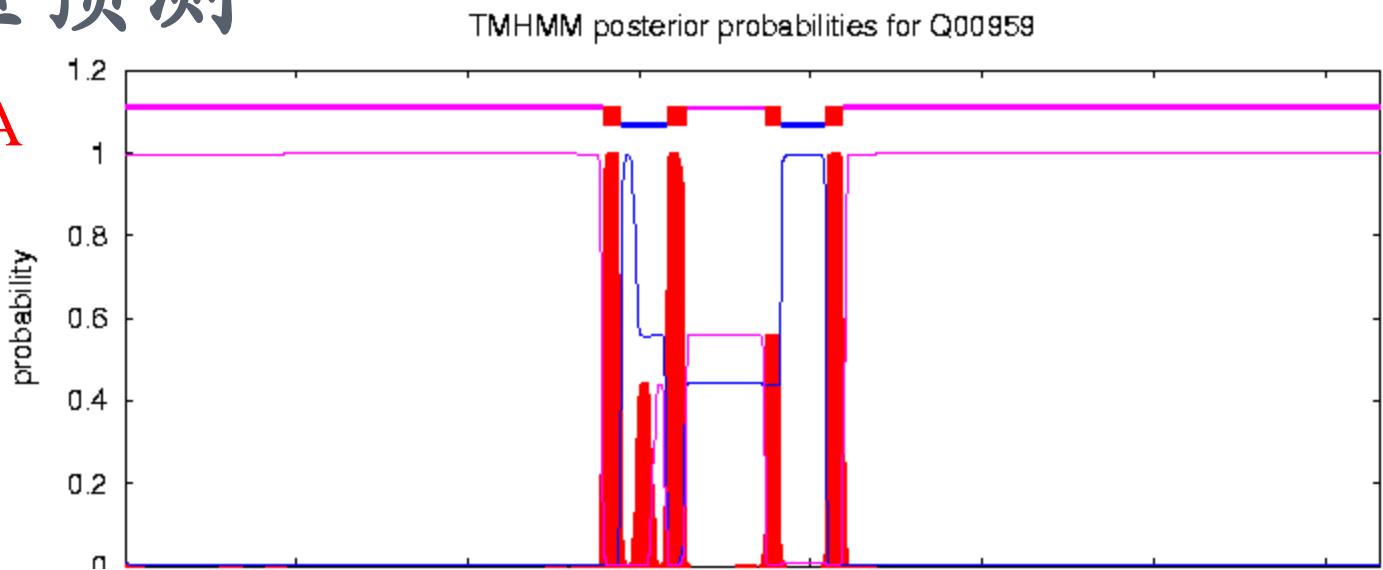


Q00960

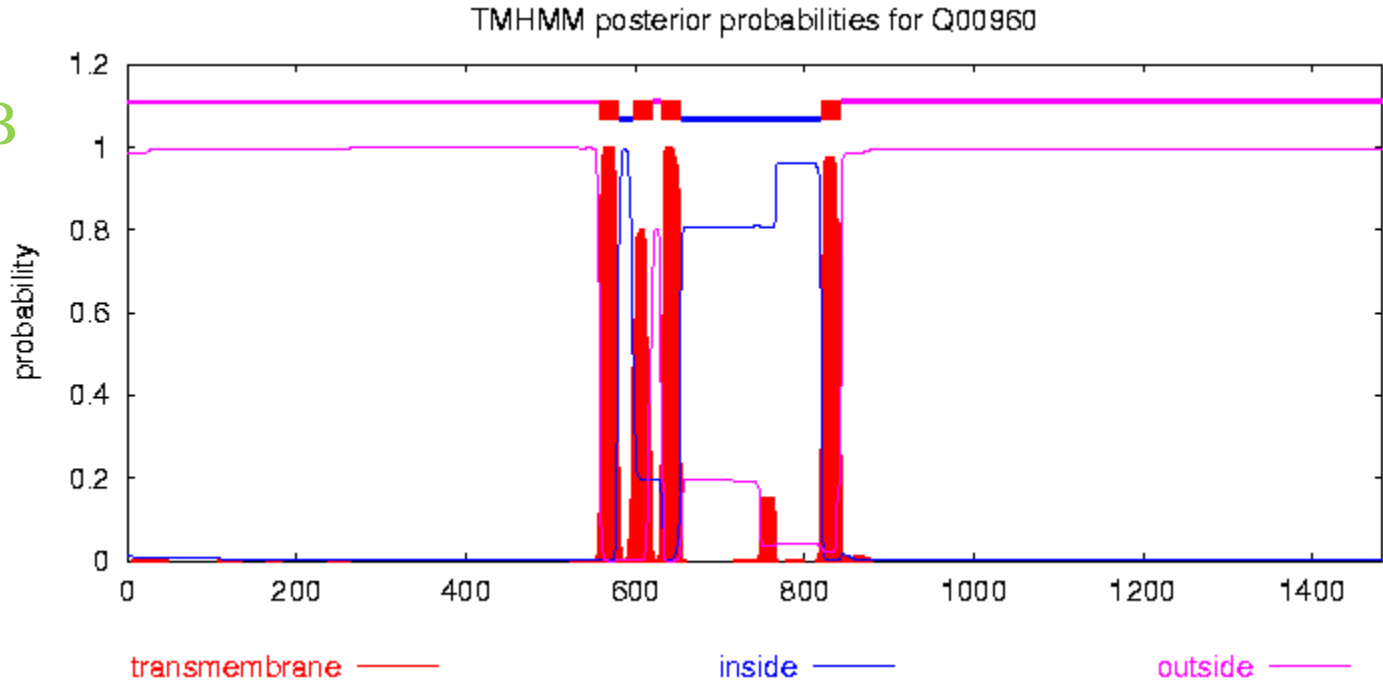


跨膜区预测

NR2A



NR2B



跨膜区预测

HMMTOP

NR2A Length: 1464

N-terminus: OUT

Number of transmembrane helices: **4**

Transmembrane helices: 557-576 629-647 747-765 817-836


NR2B Length: 1482

N-terminus: OUT

Number of transmembrane helices: **4**

Transmembrane helices: 522-539 558-577 600-617 630-648

跨膜区预测

ProtParam  - Physico-chemical parameters of a protein sequence (amino-acid and atomic compositions, isoelectric point, extinction coefficient, etc.)

NR2A

FT SIGNAL	1-22	Potential.	
FT CHAIN	23-1464	Glutamate [NMDA] receptor subunit	
FT TOPO_DOM	23-555	Extracellular (Potential).	
FT TRANSMEM	556-576	Potential.	
FT TOPO_DOM	577-633	Cytoplasmic (Potential).	1
FT TRANSMEM	634-654	Potential.	
FT TOPO_DOM	655-816	Extracellular (Potential).	2
FT TRANSMEM	817-837	Potential.	
FT TOPO_DOM	838-1464	Cytoplasmic (Potential).	3
FT REGION	511-513	Glutamate binding.	
FT REGION	689-690	Glutamate binding.	
FT MOTIF	1462-1464	PDZ-binding.	

NR2B

FT SIGNAL	1-26	Potential.	
FT CHAIN	27-1482	Glutamate [NMDA] receptor subunit	
FT TOPO_DOM	27-557	Extracellular (Potential).	
FT TRANSMEM	558-578	Potential.	
FT TOPO_DOM	579-634	Cytoplasmic (Potential).	1
FT TRANSMEM	635-655	Potential.	
FT TOPO_DOM	656-817	Extracellular (Potential).	2
FT TRANSMEM	818-838	Potential.	
FT TOPO_DOM	839-1482	Cytoplasmic (Potential).	3
FT MOTIF	1480-1482	PDZ-binding.	
FT COMPBIAS	984-989	Polv-His.	

Instability index:

The instability index (II) is computed to be 102.13
This classifies the protein as unstable.

Metal binding	128	1	Zinc <small>By similarity</small>
Metal binding	283	1	Zinc <small>By similarity</small>
Binding site	518	1	Glutamate
Binding site	731	1	Glutamate; via amide nitrogen
Site	614	1	Functional determinant of NMDA receptors

Metal binding	127	1	Zinc
Metal binding	284	1	Zinc
Site	615	1	Functional determinant of NMDA receptors

跨膜区预测小结:

	NR2A	NR2B
TAMP	8	6
SOSUI	4	6
TopPred	4	4
TMHMM	4	4
HMMTOP	4	4
PrptParam	3	3

NR2A和NR2B各有四个跨膜区

二级结构预测

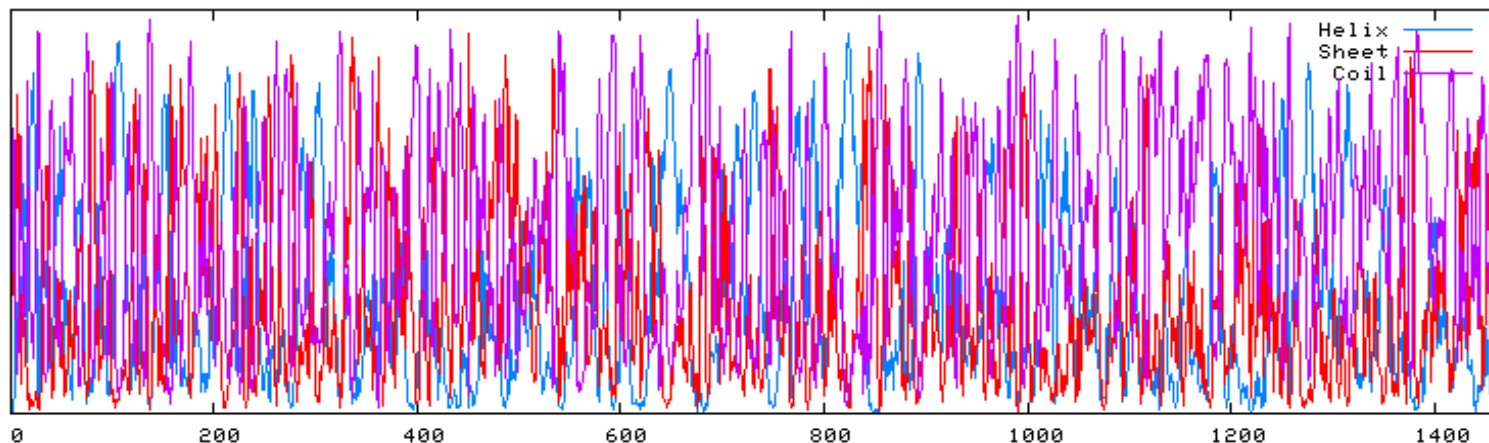
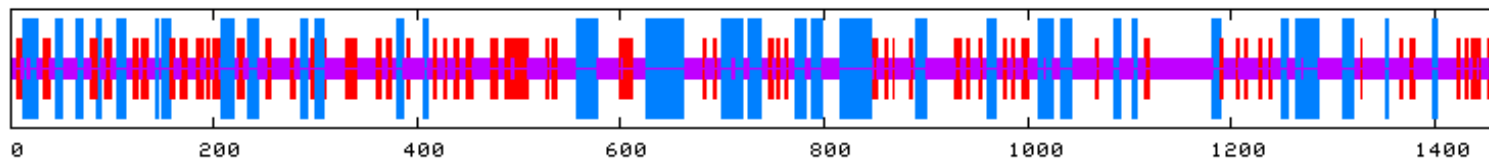
GOR4

NR2A

GOR4 :

Alpha helix	(Hh)	:	371	is	25.34%
<u>3₁₀ helix</u>	(Gg)	:	0	is	0.00%
Pi helix	(Ii)	:	0	is	0.00%
Beta bridge	(Bb)	:	0	is	0.00%
Extended strand	(Ee)	:	292	is	19.95%
<u>Beta turn</u>	(Tt)	:	0	is	0.00%
Bend region	(Ss)	:	0	is	0.00%
Random coil	(Cc)	:	801	is	54.71%
<u>Ambiguous states</u>	(?)	:	0	is	0.00%
Other states		:	0	is	0.00%

蓝色条带表示可能的 α 螺旋结构，
红色条带表示可能的beta折叠，
预测得到的 α 螺旋占整个序列的
25.34%，beta折叠占19.95%。



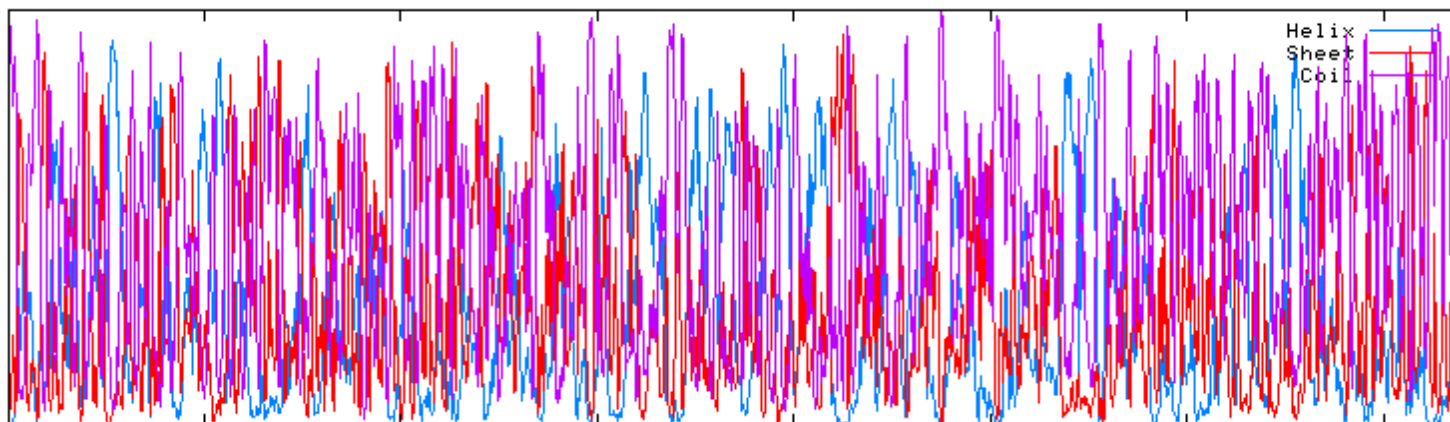
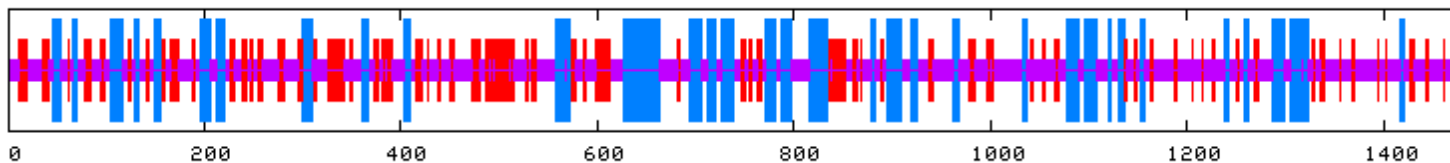
二级结构预测

GOR4 :

Alpha helix (Hh)	:	343 is	23.14%
3 ₁₀ helix (Gg)	:	0 is	0.00%
Pi helix (Ii)	:	0 is	0.00%
Beta bridge (Bb)	:	0 is	0.00%
Extended strand (Ee)	:	334 is	22.54%
Beta turn (Tt)	:	0 is	0.00%
Bend region (Ss)	:	0 is	0.00%
Random coil (Cc)	:	805 is	54.32%
Ambiguous states (?)	:	0 is	0.00%
Other states	:	0 is	0.00%

NR2B

预测得到的 α 螺旋占整个序列的23.14%，beta折叠占22.54%。



二级结构预测

HNN

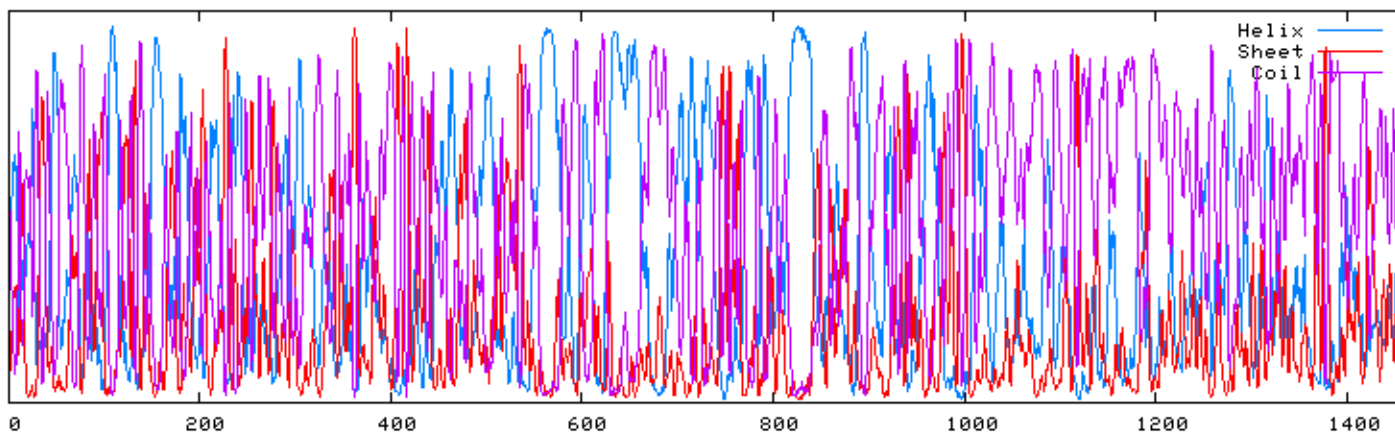
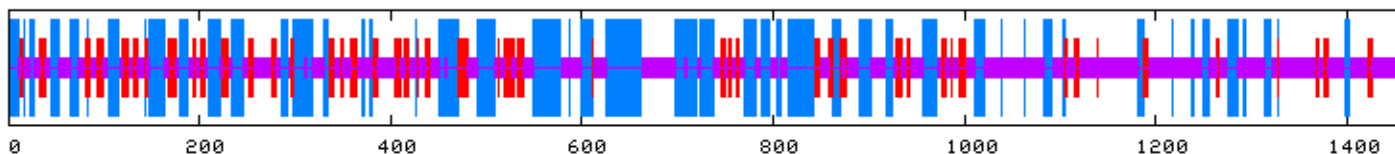
Sequence length : 1464

NR2A

HNN :

Alpha helix	(Hh)	:	449	is	30.67%
3 ₁₀ helix	(Gg)	:	0	is	0.00%
Pi helix	(Ii)	:	0	is	0.00%
Beta bridge	(Bb)	:	0	is	0.00%
Extended strand	(Ee)	:	224	is	15.30%
Beta turn	(Tt)	:	0	is	0.00%
Bend region	(Ss)	:	0	is	0.00%
Random coil	(Cc)	:	791	is	54.03%
Ambiguous states (?)		:	0	is	0.00%
Other states		:	0	is	0.00%

蓝色条带表示可能的 α 螺旋结构，
红色条带表示可能的beta折叠，
预测得到的 α 螺旋占整个序列的
30.67%，beta折叠占15.30%。



二级结构预测

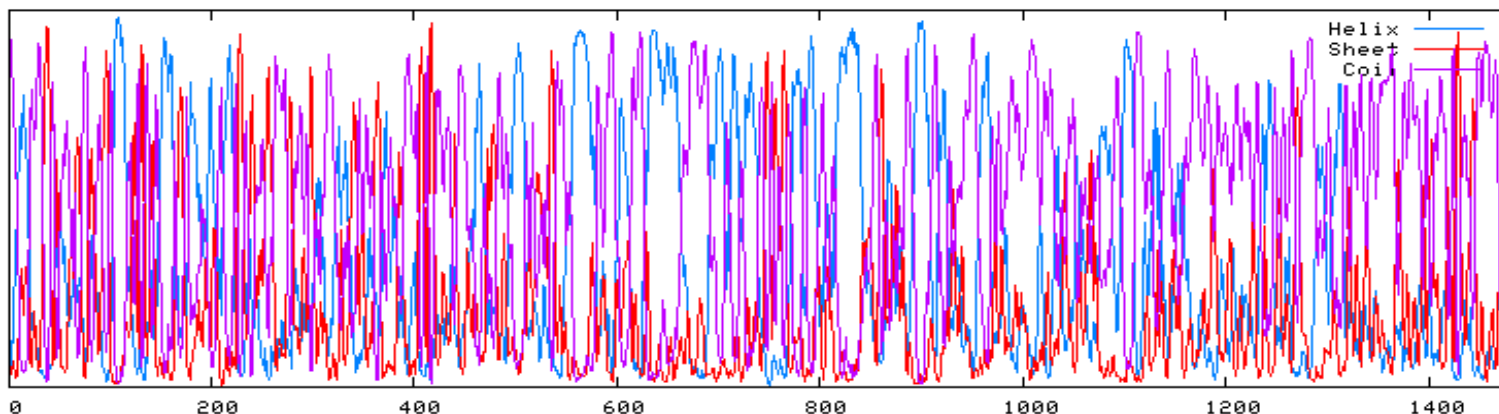
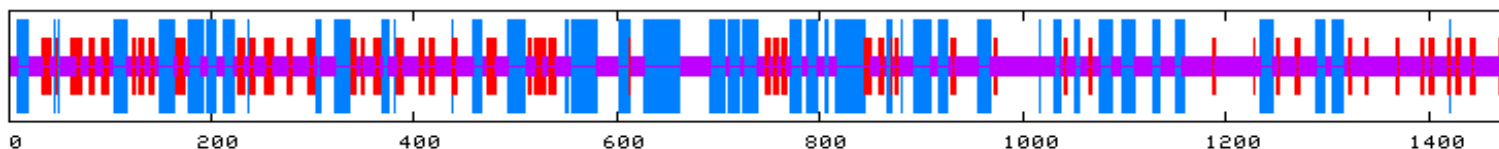
Sequence length : 1482

NR2B

HMM :

Alpha helix	(Hh)	:	435	is	29.35%
3 ₁₀ helix	(Gg)	:	0	is	0.00%
Pi helix	(Ii)	:	0	is	0.00%
Beta bridge	(Bb)	:	0	is	0.00%
Extended strand	(Ee)	:	236	is	15.92%
Beta turn	(Tt)	:	0	is	0.00%
Bend region	(Ss)	:	0	is	0.00%
Random coil	(Cc)	:	811	is	54.72%
Ambiguous states (?)		:	0	is	0.00%
Other states		:	0	is	0.00%

预测得到的 α 螺旋占整个序列的29.35%，beta折叠占15.92%。



二级结构预测 SOPMA

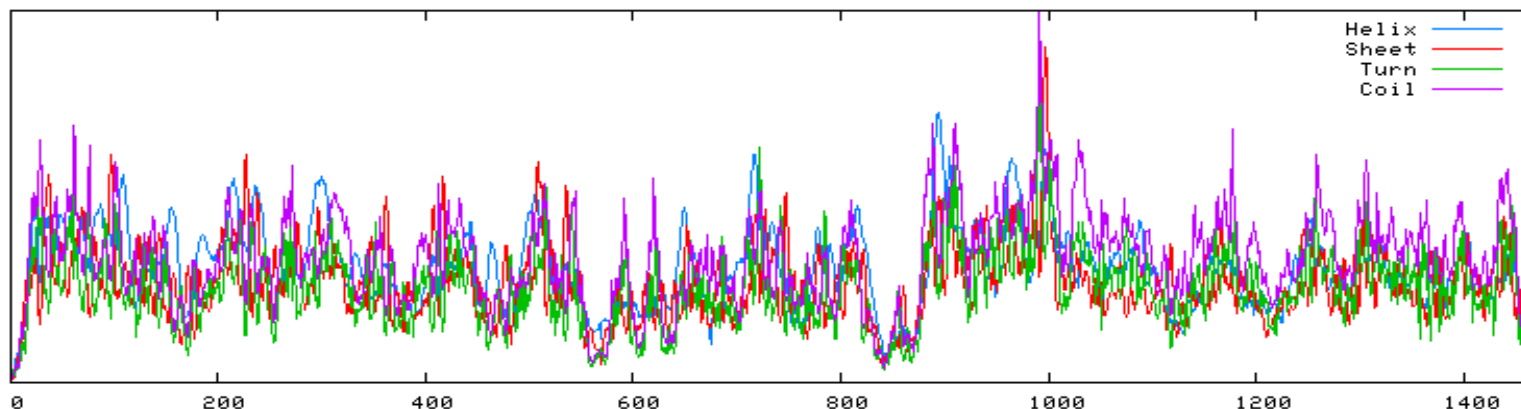
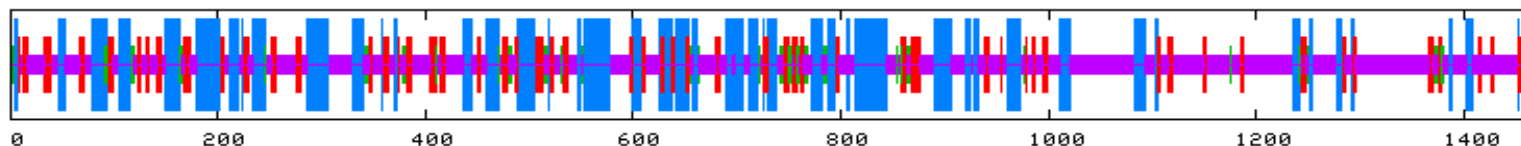
Sequence length : 1464

SOPMA :

Alpha helix	(Hh)	:	427	is	29.17%
3 ₁₀ helix	(Gg)	:	0	is	0.00%
Pi helix	(Ii)	:	0	is	0.00%
Beta bridge	(Bb)	:	0	is	0.00%
Extended strand	(Ee)	:	223	is	15.23%
Beta turn	(Tt)	:	54	is	3.69%
Bend region	(Ss)	:	0	is	0.00%
Random coil	(Cc)	:	760	is	51.91%
Ambiguous states (?)		:	0	is	0.00%
Other states		:	0	is	0.00%

NR2A

蓝色条带表示可能的 α 螺旋结构，
红色条带表示可能的beta折叠，
预测得到的 α 螺旋占整个序列的
29.17%，beta折叠占15.23%。



二级结构预测

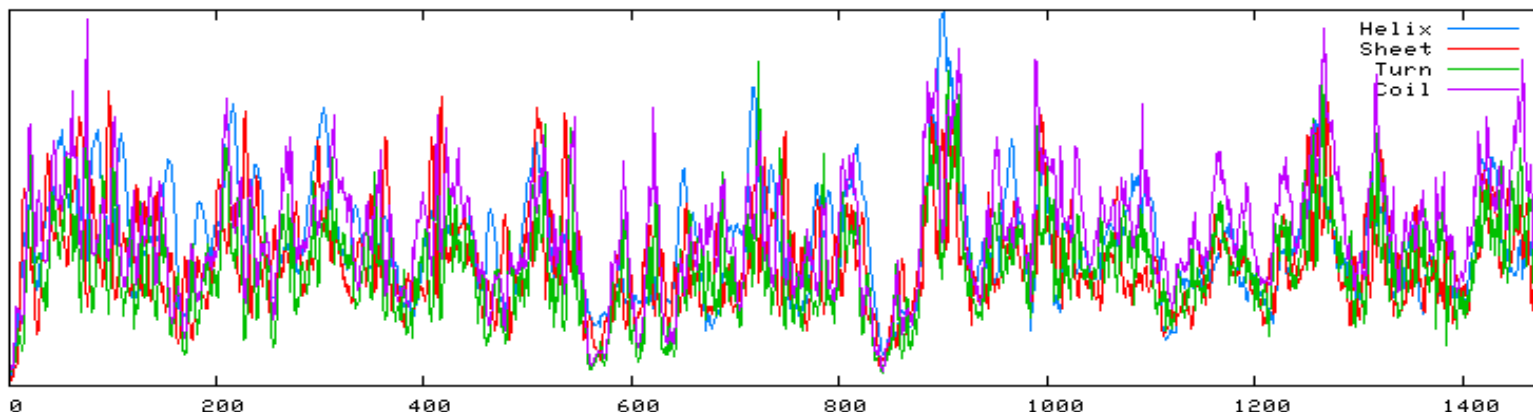
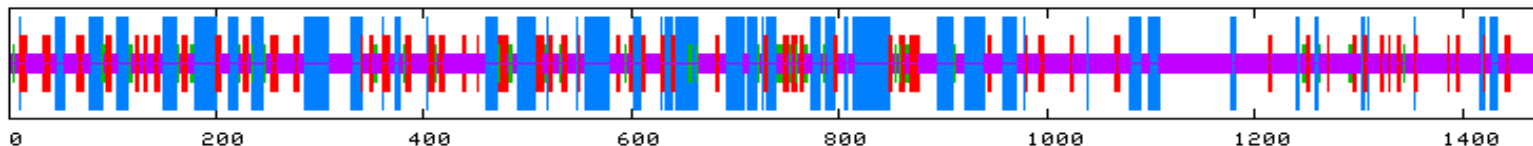
Sequence length : 1482

NR2B

SOPMA :

Alpha helix	(Hh)	:	426	is	28.74%
3 ₁₀ helix	(Gg)	:	0	is	0.00%
Pi helix	(Ii)	:	0	is	0.00%
Beta bridge	(Bb)	:	0	is	0.00%
Extended strand	(Ee)	:	229	is	15.45%
Beta turn	(Tt)	:	62	is	4.18%
Bend region	(Ss)	:	0	is	0.00%
Random coil	(Cc)	:	765	is	51.62%
Ambiguous states (?)		:	0	is	0.00%
Other states		:	0	is	0.00%

预测得到的 α 螺旋占整个序列的28.74%，beta折叠占15.45%。



二级结构预测小结

Alpha helix

	NR2A	NR2B
GOR4	25.34%	23.14%
HNN	30.67%	29.35%
SOPMA	29.17%	28.74%

Beta strand

	NR2A	NR2B
GOR4	19.95%	22.54%
HNN	15.30%	15.92%
SOPMA	15.23%	15.45%

NR2A, NR2B二级结构几乎没有区别。

三、翻译后修饰位点预测 及蛋白相互作用分析

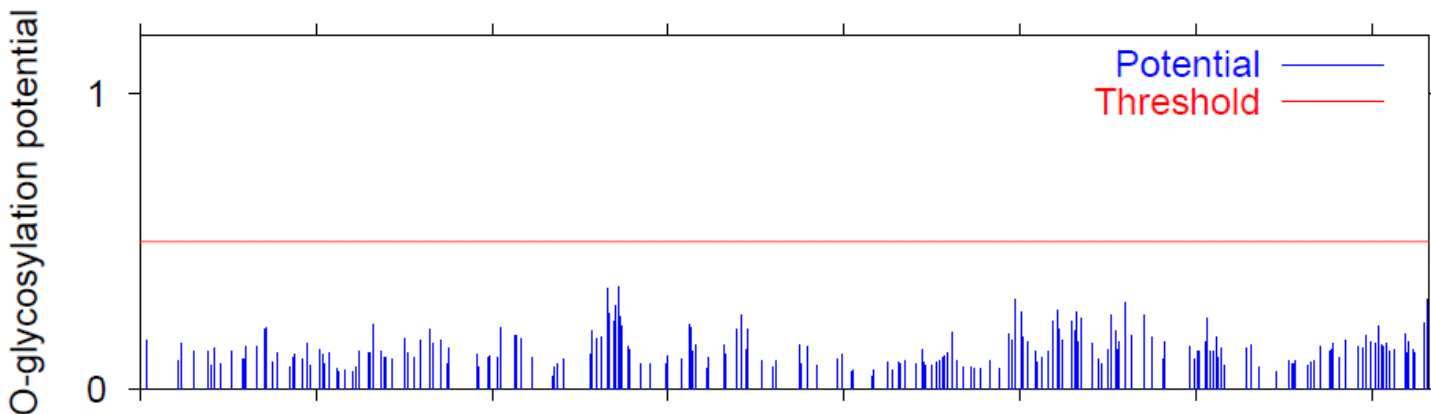
(一) 蛋白修饰预测

- O-糖基化: NetOGlyc
- N-糖基化: NetNGlyc
- 蛋白酶体降解位点: Prop
- 泛素化位点: SUMOsp
- 磷酸化: Netphos ,Netphos K
PhosphoSite database

翻译后修饰(O糖基化)预测

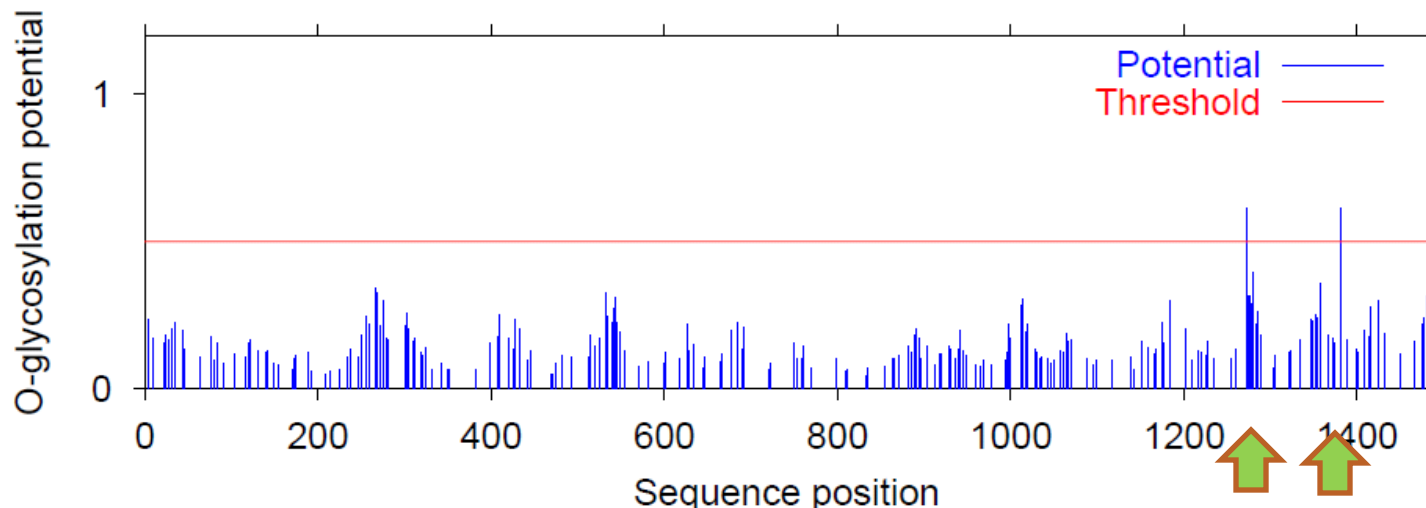
NetOGlyc 3.1: predicted O-glycosylation sites in Q00959

NR2A



NetOGlyc 3.1: predicted O-glycosylation sites in Q00960

NR2B

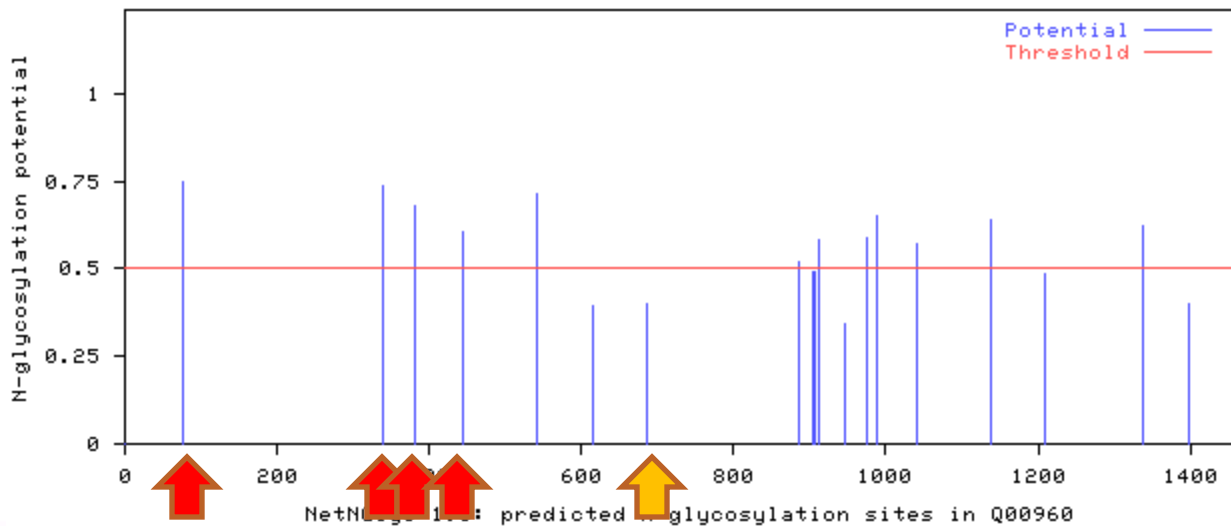


O糖基化发生在多肽链上丝、苏、酪氨酸或羟赖、羟脯氨酸的羟基氧原子上。

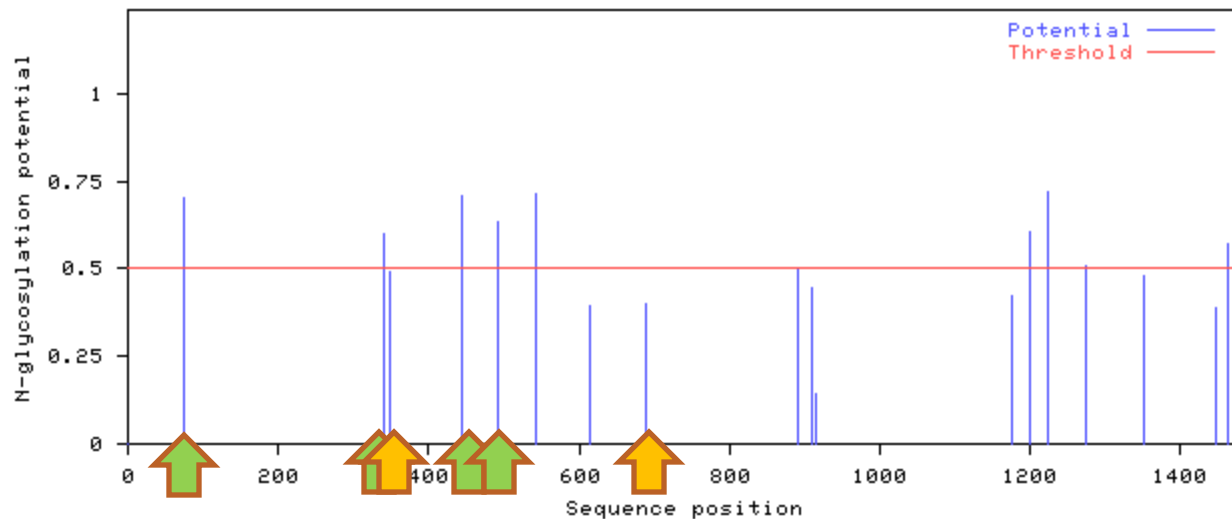
翻译后修饰(N糖基化)预测

NetNGlyc 1.0: predicted N-glycosylation sites in Q00959

NR2A



NR2B



N糖基化发生在位于蛋白ASN.XAA.SER/THR(XAA为除脯氨酸外的氨基酸残基)序列上的天冬酰胺上

泛素化位点预测

NR2A

Position	Peptide	Score	Cutoff	Type
214	EDA K TQV	3.044	2.64	Typell: Non-consensus
326	QA E KPET	3.176	2.64	Typell: Non-consensus
804	HNE K NEV	2.941	2.64	Typell: Non-consensus
1047	HSL K SPR	2.765	2.64	Typell: Non-consensus

Enter sequence(s) in FASTA format

NR2B

Position	Peptide	Score	Cutoff	Type
30	RSQ K SPP	2.456	2.26	Typell: Non-consensus
137	MAD K DES	2.706	2.26	Typell: Non-consensus
221	NQL K KLQ	2.765	2.26	Typell: Non-consensus
445	SEN K TDE	2.338	2.26	Typell: Non-consensus
805	HNE K NEV	2.941	2.26	Typell: Non-consensus
1031	PSS K HSQ	2.603	2.26	Typell: Non-consensus
1079	NA A KRRK	2.515	2.26	Typell: Non-consensus
1082	KRR K QQY	2.676	2.26	Typell: Non-consensus
1163	DDF K RDS	2.471	2.26	Typell: Non-consensus
1292	KA Q KKNR	2.676	2.26	Typell: Non-consensus
1312	DLQ K EEA	3.309	2.26	Typell: Non-consensus

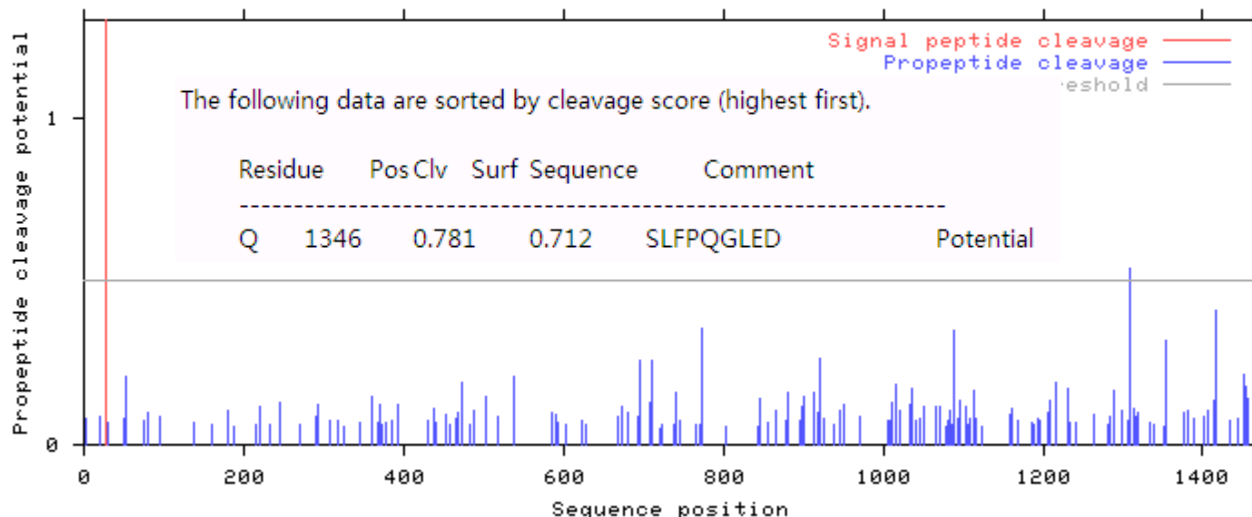
Enter sequence(s) in FASTA format

Q00960 NR2B

蛋白酶体水解位点预测

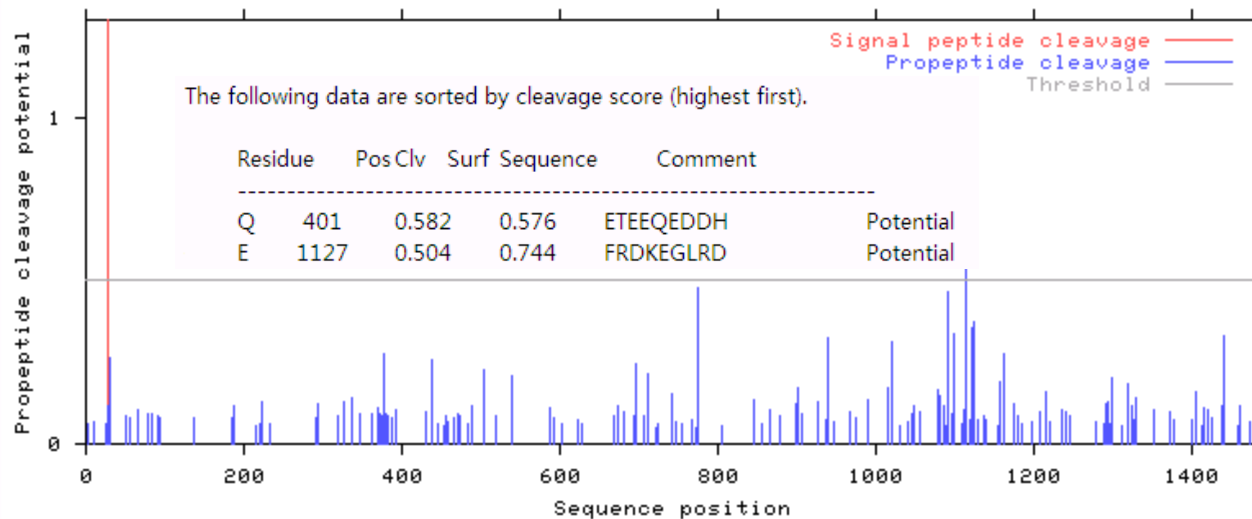
NR2A

ProP 1.0: predicted propeptide cleavage sites in Q00959, furin-specific prediction



NR2B

ProP 1.0: predicted propeptide cleavage sites in Q00960, furin-specific prediction



翻译后修饰预测小结

NR2A NR2B

O-糖基化:	0	2	细胞外分泌,通过形成蛋白多糖黏附细胞参与黏膜分泌
N-糖基化	4	4	与蛋白折叠有关,只发生在胞外段
泛素化	4	11	NR2B降解速度可能更快
蛋白酶体水解	1	2	NR2B降解速度可能更快

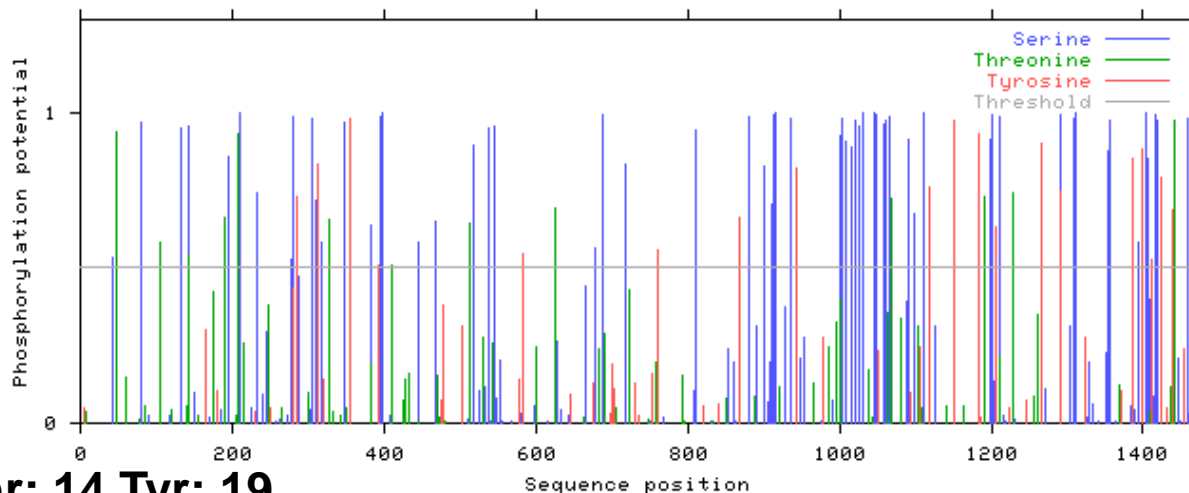
磷酸化位点预测意义

- 与信号转导密切相关
- 可以作为干扰受体功能的靶位点。例如已应用于研究的干扰肽TAT-GluR2_3Y就是干扰GluR2的C末端磷酸化位点Y873，从而影响受体功能。

翻译后修饰(磷酸化)预测

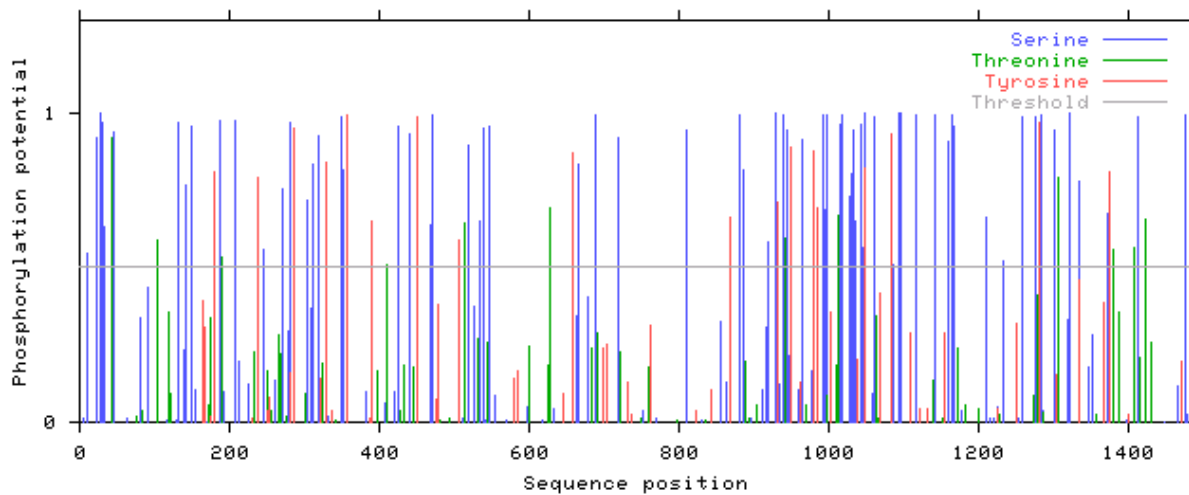
NetPhos 2.0: predicted phosphorylation sites in Q00959

NR2A



NetPhos 2.0: predicted phosphorylation sites in Q00960

NR2B



NetPhosK - Kinase specific phosphorylation sites in eukaryotic proteins

Threshold:

NR2A

NR2B

>0.7

S-1020	PKC	0.82
S-1025	PKA	0.76
S-1046	PKC	0.72

T-1152	PKC	0.74
S-1323	PKC	0.85

0.6-0.7

S-890	DNAPK	0.65
S-900	PKC	0.64
S-1232	cdk5	0.68

S-882	PKA	0.65
-------	-----	------

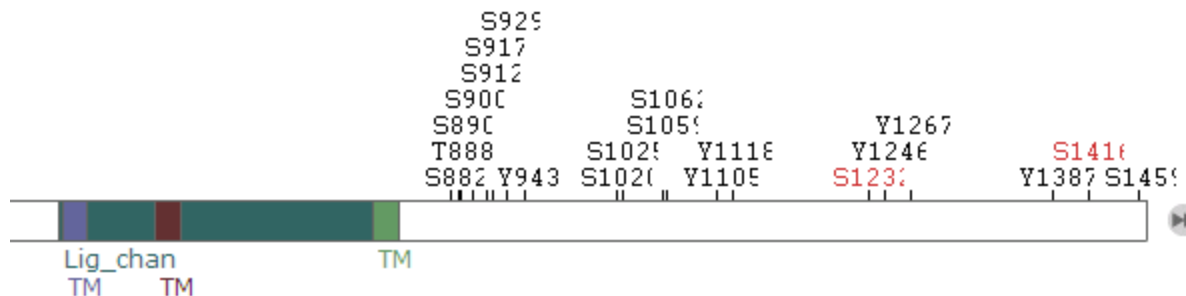
0.5-0.6

S-890	ATM	0.55
S-890	cdc2	0.55
S-900	cdc2	0.51
S-917	RSK	0.52
S-917	GSK3	0.50
S-917	cdk5	0.59
S-929	cdc2	0.52
Y-943	INSR	0.50
S-1059	CKII	0.58
S-1059	cdc2	0.53
S-1416	PKA	0.59

S-886	cdk5	0.50
S-917	p38MAPK	0.56
S-917	cdk5	0.53
S-930	RSK	0.54
T-1152	CKII	0.55
S-1168	CKI	0.57
S-1220	cdc2	0.53
S-1303	RSK	0.51
S-1303	PKA	0.56
S-1480	CKII	0.56

翻译后修饰(磷酸化)位点

NR2A

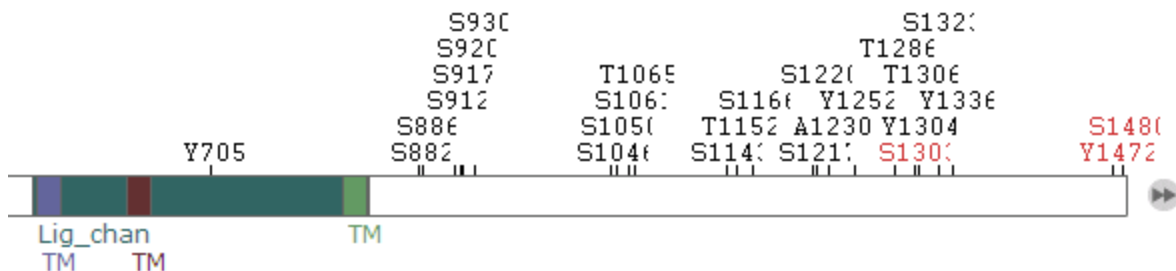


Sites Implicated In

activation: **S1232-p**

regulates molecular association: **S1416-p**

NR2B



Sites Implicated In

altered intracellular location: **S1303-p**

receptor internalization: **S1480-p**

regulates molecular association: **S1303-p, Y1472-p, S1480-p**

翻译后修饰(磷酸化)小结

预测结果

数据库信息

NR2A

Ser:62
Thr: 14
Tyr: 19

Ser1232:激活受体作用(CDK5)
Ser1416: 调节分子结合(PKC)

NR2B

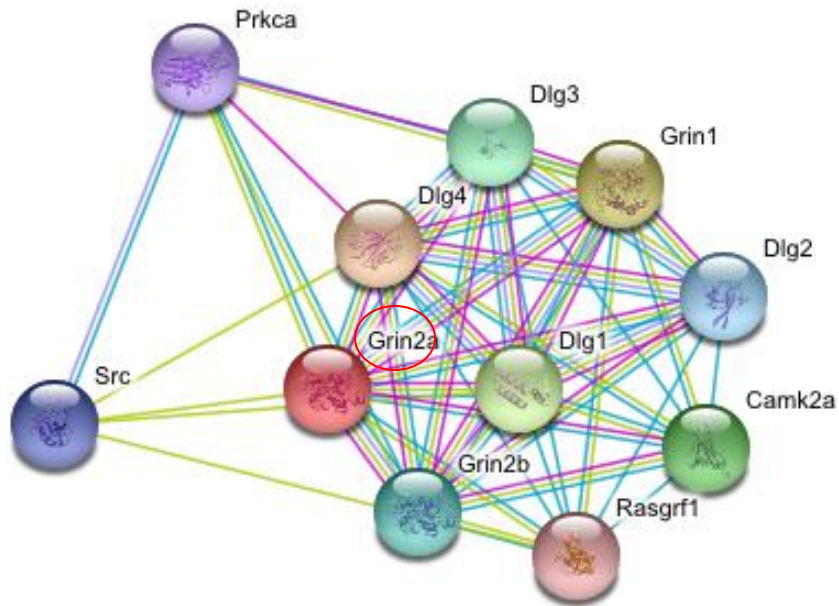
Ser: 73
Thr: 12
Tyr: 18

Ser1303: 调节分子结合,
细胞亚定位 (CaMK2)
Tyr1472: 调节分子连接 (PSD-95)
Ser1480: 调节分子连接
受体内化 (CK2-A1)

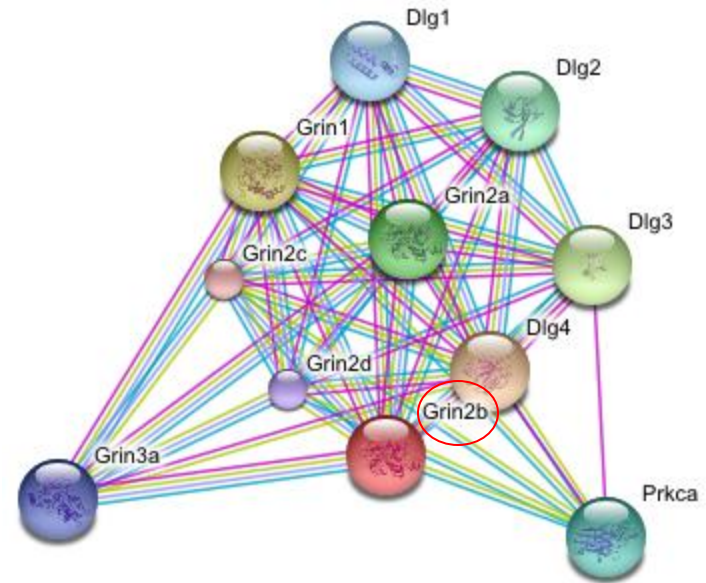
(二) 蛋白相互作用分析

STRING

NR2A



NR2B



NR2A

Grin2a: Glutamate [NMDA] receptor subunit epsilon-1 (Q00959)

found to interact with 11 partner(s):

protein	evidences	score	direct.	ass.	coloc.	enz.	complex.	HT.
x Dlg4 <i>Rattus norvegicus</i> (P31016)	6	0.91		6				
x Dlg1 <i>Rattus norvegicus</i> (Q62696)	2	0.64		2				
x Flot1 <i>Rattus norvegicus</i> (Q9Z1E1)	3	0.57		2	1		1	
x Camk2a <i>Rattus norvegicus</i> (P11275)	2	0.48		2				
x Magi2 <i>Rattus norvegicus</i> (O88382)	2	0.48		1	1			
x Dlg2 <i>Rattus norvegicus</i> (Q63622)	1	0.43		1				
x Flot1 <i>Mus musculus</i> (O08917)	1	0.43		1				
x Grip2 <i>Rattus norvegicus</i> (Q9WTW1)	1	0.43		1				
x Flot2 <i>Rattus norvegicus</i> (Q9Z2S9)	3	0.31		2	1		3	
x Grin2b <i>Rattus norvegicus</i> (Q00960)	4	0.31		2	2		4	
x Grin1 <i>Rattus norvegicus</i> (P35439)	1	0.28		1				

Grin2b: Glutamate [NMDA] receptor subunit epsilon-2 (Q00960)

found to interact with 18 partner(s):

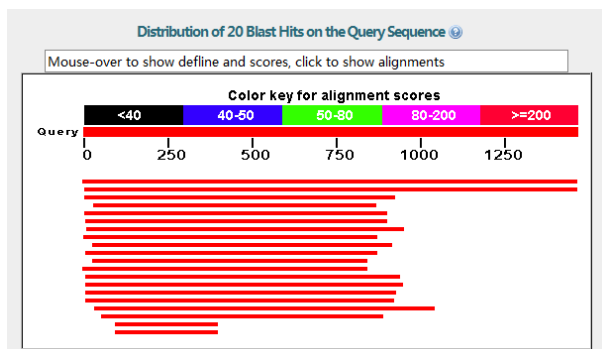
protein	evidences	score	direct.	ass.	coloc.	enz.	complex.	HT.
x Dlg4 <i>Rattus norvegicus</i> (P31016)	5	0.78		4	1			
x Dlg3 <i>Rattus norvegicus</i> (Q62936)	5	0.67	3	2				
x Camk2a <i>Mus musculus</i> (P11798)	3	0.64	1	2				
x Lin7b <i>Rattus norvegicus</i> (Q9Z252)	5	0.59		4	1			
x Flot1 <i>Rattus norvegicus</i> (Q9Z1E1)	3	0.57		2	1		1	
x Inadl <i>Mus musculus</i> (Q63ZW7)	4	0.55		4				3
x Flot2 <i>Rattus norvegicus</i> (Q9Z2S9)	4	0.51		3	1		3	
x Grin1 <i>Rattus norvegicus</i> (P35439)	2	0.48		2				
x Dlg2 <i>Rattus norvegicus</i> (Q63622)	1	0.43		1				
x Dlg4 <i>Mus musculus</i> (Q62108)	1	0.43		1				1
x Flot1 <i>Mus musculus</i> (O08917)	1	0.43		1				
x Il16 <i>Mus musculus</i> (O54824)	1	0.43		1				
x q7jfn4_pig <i>Sus scrofa</i> (Q7JFN4)	1	0.43	1					
x q91587_xenla <i>Xenopus laevis</i> (Q91587)	1	0.43	1					
x Grin2a <i>Rattus norvegicus</i> (Q00959)	4	0.31		2	2		4	
x Lrrc7 <i>Rattus norvegicus</i> (P70587)	1	0.28		1				
x Src <i>Mus musculus</i> (P05480)	1	0.28		1				
x p15791-2 <i>Rattus norvegicus</i> (P15791-2)	1	0	1					

NR2B

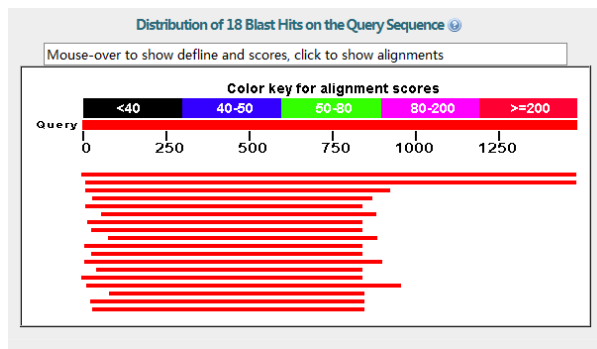
四、进化关系分析

获取序列 (BLAST)

NR2A



NR2B



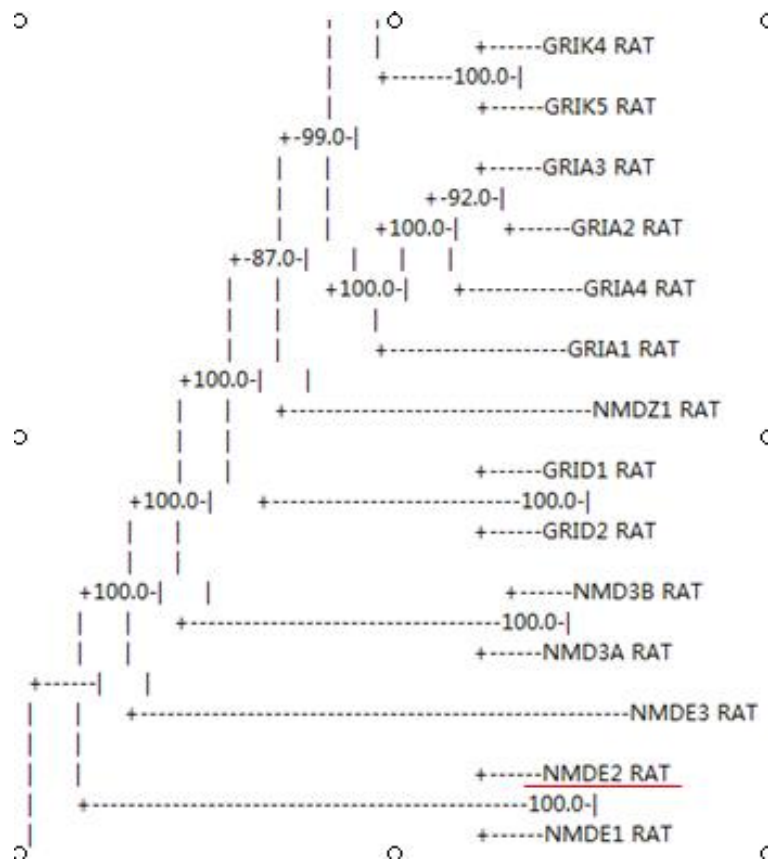
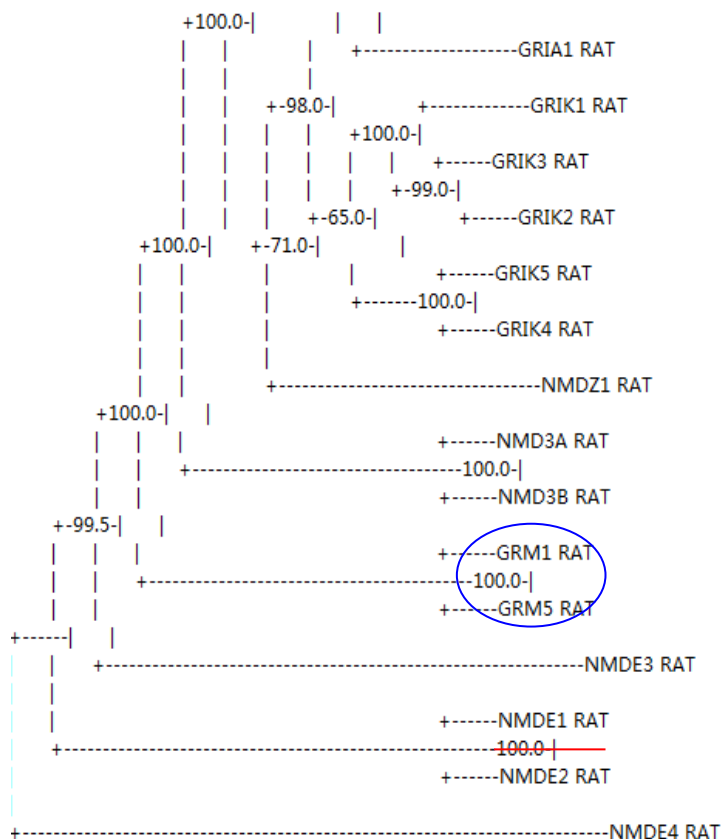
Database: Swissprot protein sequences,
organism: rattus norvegicus,
Algorithm: PSI-BLAST, expect threshold:0.01,
word size:2。

运行程序，重复三次以使系统选择最适算法

建立进化树 (WebLab protocol)

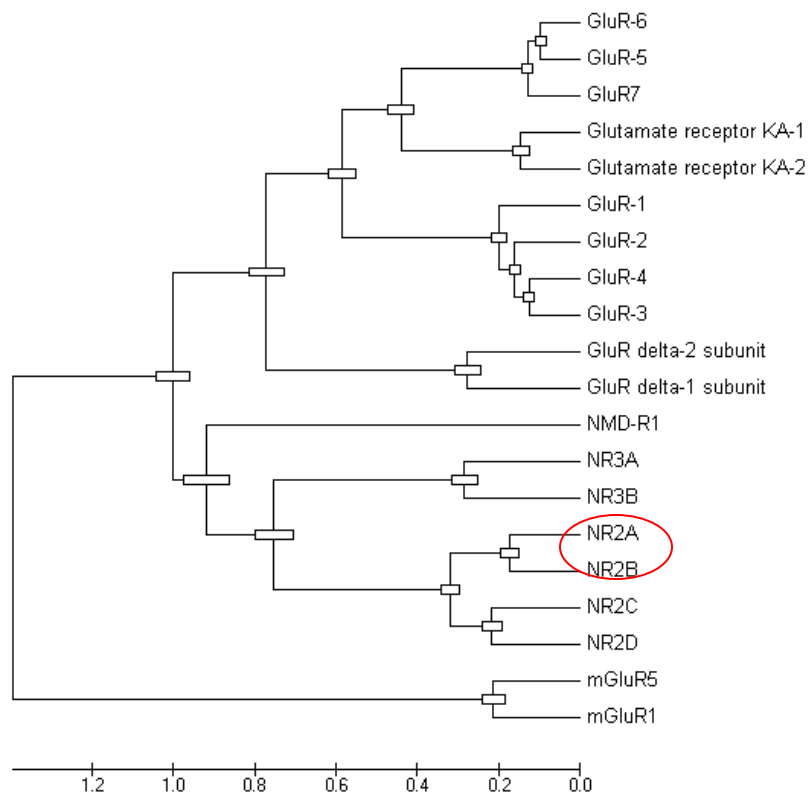
NR2A 19个蛋白

NR2B 17个蛋白

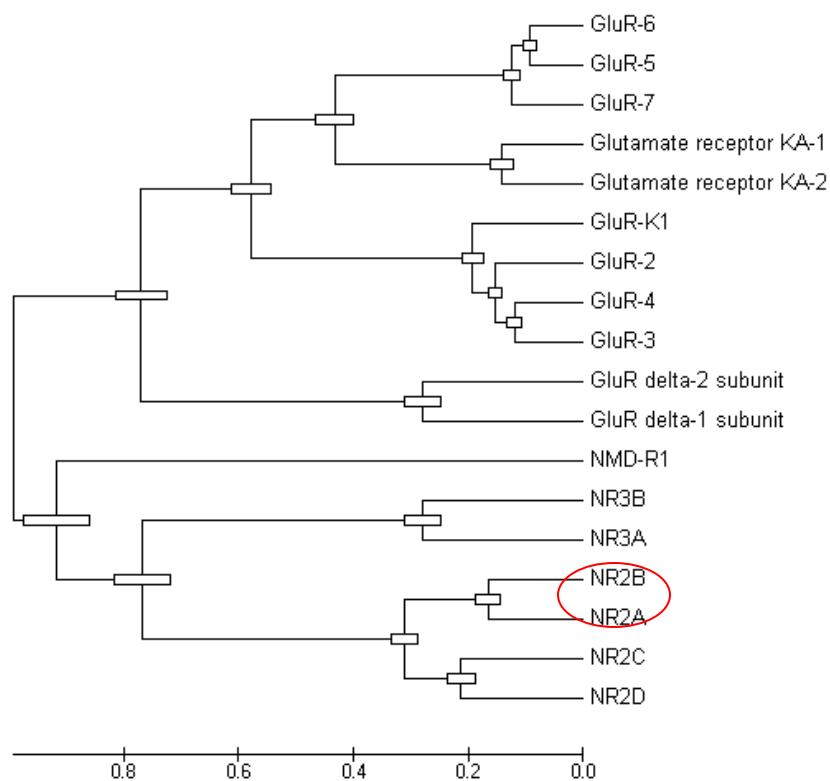


建立进化树 (MEGA:最大简约法)

NR2A



NR2B



NR2A与NR2B进化关系很近。

其他与之相近的蛋白也是谷氨酸受体，
包括kainate receptor、AMPA receptor等离子型受体亚基。

NR2A还与代谢型谷氨酸受体亚基mGluR1、mGluR5相近。

五、空间结构分析

PDB 信息:

1PB8: NR1 ligand binding core

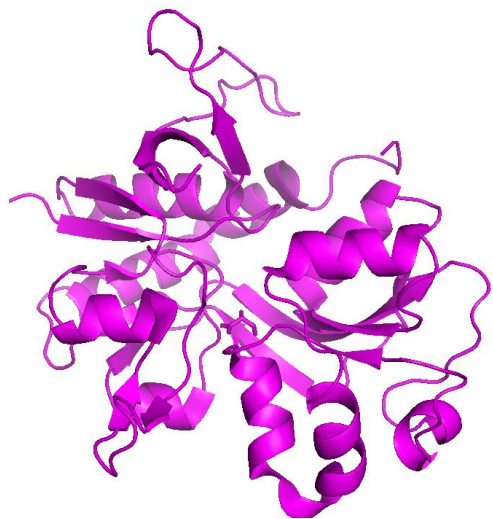
2A5S: NR2A ligand binding core

2A5T: NR1-NR2 ligand binding core
complex

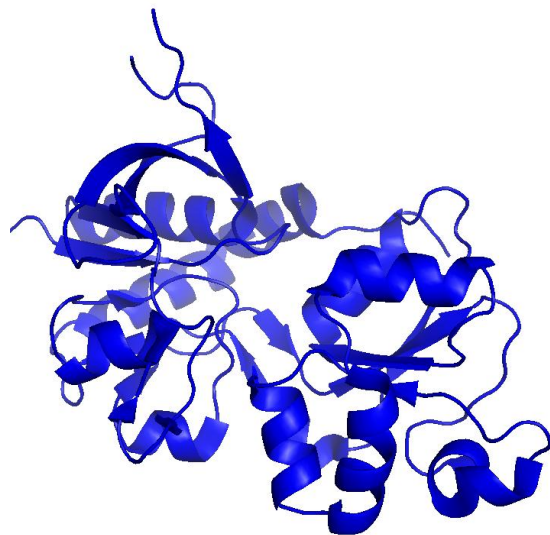
3JPW: amino-terminal domain of NR2B

工具: PyMOL ; docking

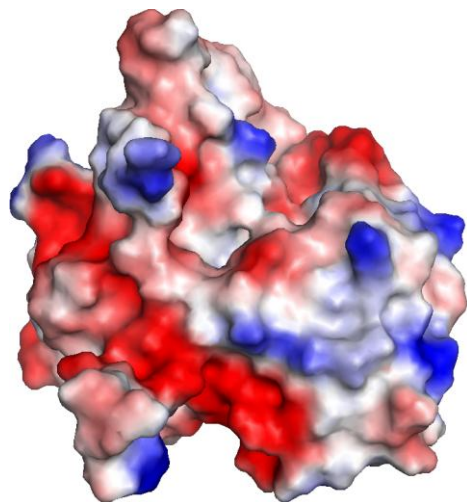
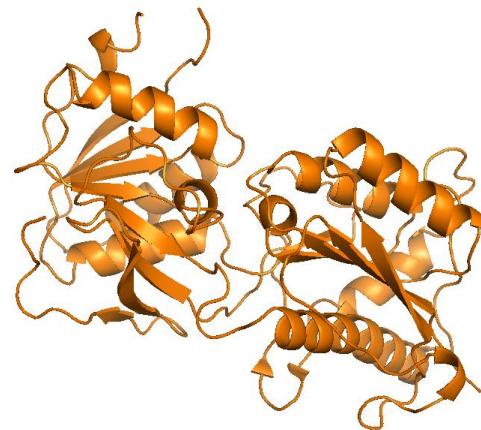
NR1



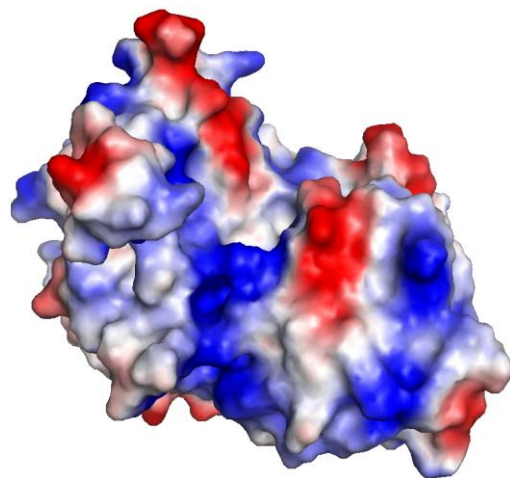
NR2A



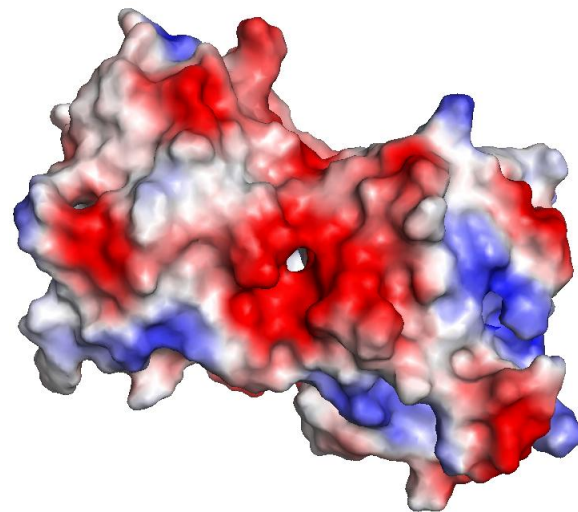
NR2B



1PB8



2A5S

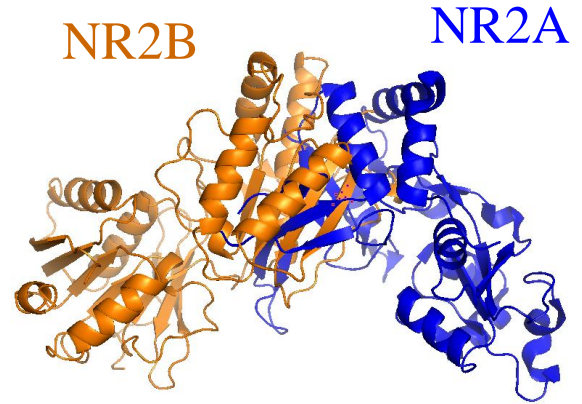


3JPW

直接比较NR2A与NR2B:

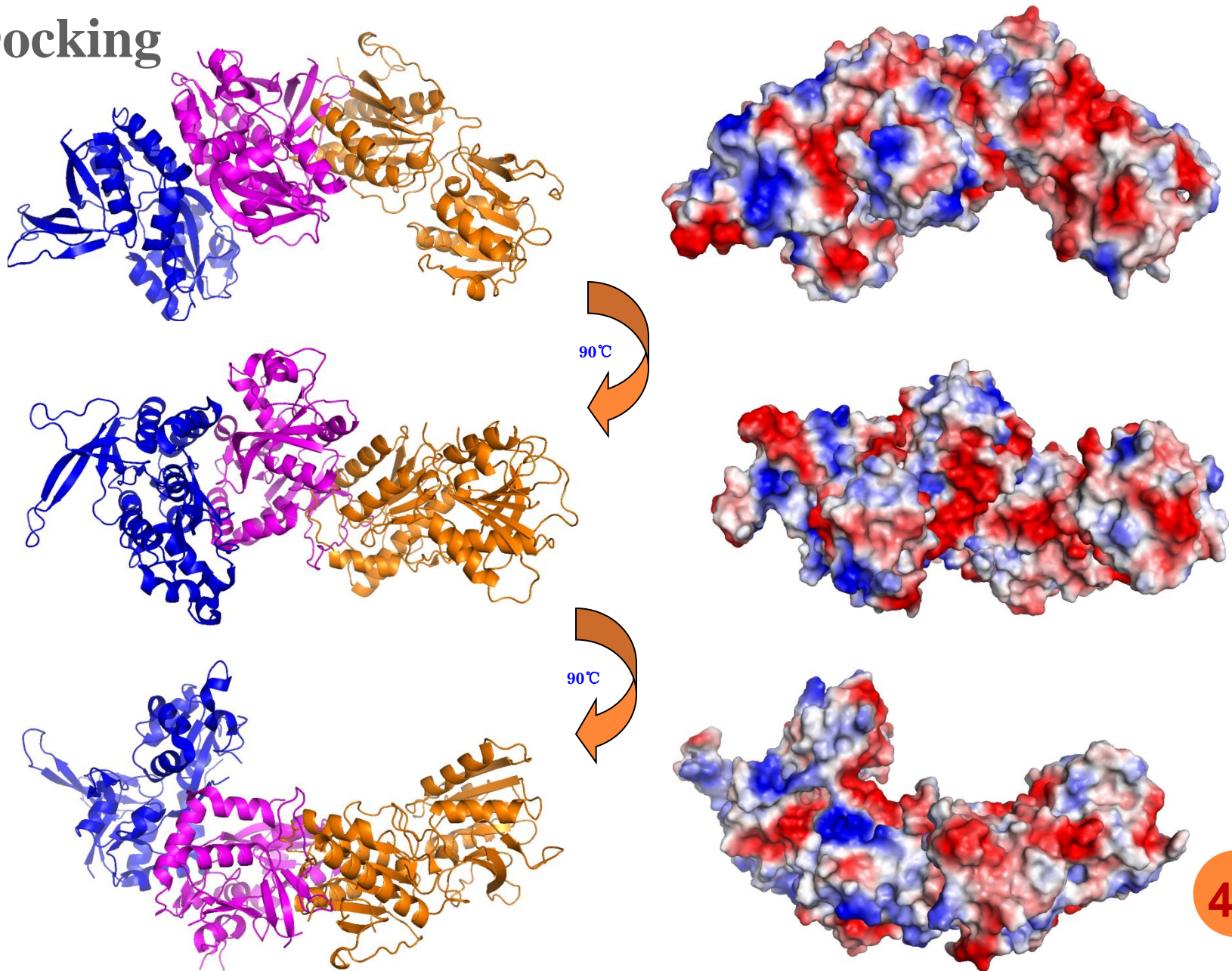
```

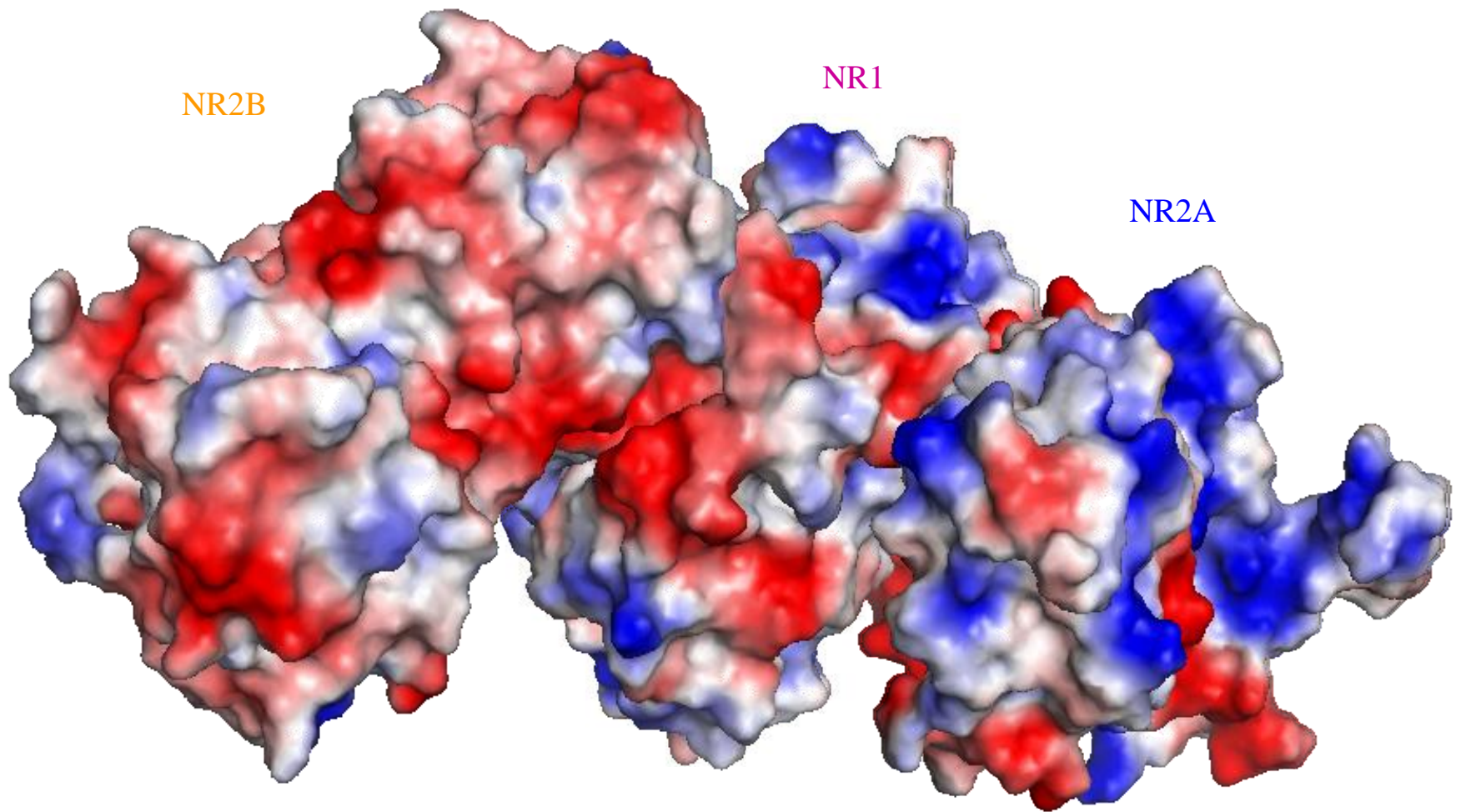
2A5S_A|G PDDNHLSIVTLEEAPFVIVEDIDPLTETCVRNTVPCRKFKVINNSTNEGMNVKKC---- 56
3JPW_A|- PPSIGIAVILVGTSDVEAIKDAHEKDDFHHLSSVPRVELVAMNETDPKSIITRICDLMS 59
      * .  : : : : : * : * . : . . * * : * : * : : : : *
2A5S_A|-----CKGFCCI 62
3JPW_A|DRKIQGVVFADDDTQEAIQAQLDFISAQTLTPILGIHGGSSMIMADKDESSMFFQFGPSL 119
      * *
2A5S_A|DILKKSRTVKFTYDLYLVTNG-----KHGKKVNNVWNGMIGEVV-YQRAVMAVGSLTIN 116
3JPW_A|EQQASVMLNIMEEYDLYIFSIVTTYFPGYQDFVVKIRSTIENSFVWGELEEVLLLDMSLD 179
      : : : : * * * : : : . . * * : : : . . . * : : : : : : :
2A5S_A|EERSEVVDVFSVPFVETGIVSMVSRGTQVTGLSDKKFQRPHDYSPFFRFGTVPNGSTERNI 176
3JPW_A|DGDSKIQNQLKRLQSPIILLYCTKEEATYIFEVANSVGLTGYGYTWIVPSLVAGDIDT-V 238
      : * : : : : * : : : : : : : : : : * : : : : * * : :
2A5S_A|RNNYF--YMHQYMRFNQ---RGVEDALVSLKTGKLDAFIYDAAVLNKAG----RDEGC 227
3JPW_A|PSEFFETGLISVSYDEWDYGLPARVRDGIATITTAASDMLSEHSFIPEPKSSCYNTHEKRI 298
      : : * : : : : * : : : : * : : : : : : : : : : * : : : :
2A5S_A|KLVTIGSGYIFATGYGIALQKGGSP-WKRQIDLALLQFVGDGEMEELETLWLTGICHN-- 284
3JPW_A|YQSNMLNRYLINVTFEGRDLSFSSEGDGYQMHPKLVIIILLNKERKWERVGGKWKDKSLQMKYY 358
      : : . * : : * * * . . : : : * : : : : : : * : : . : : :
2A5S_A|----- 284
3JPW_A|VWPRM 363
    
```



NR2A与NR2B的氨基端相似性不高

Docking





NR2A和NR2B有各自与NR1结合的位点，结构预测结果有待实验验证。

总结

- NR2A与NR2B在一级结构上相似度较高；
- 预测NR2A与NR2B均有4个跨膜螺旋，二级结构相差不大；
- NR2A与NR2B的糖基化修饰类似，磷酸化、泛素化及蛋白酶体降解位点NR2B较多；与NR2B有相互作用的蛋白较多；
- NR2A与NR2B的进化关系很近；
- NR2A和NR2B与NR1有不同的结点位点。

任务分配

文献检索	高珊
序列比对	王云凤
跨膜螺旋预测	马祥 马寅燕
二级结构预测	马祥
蛋白修饰和相互作用分析	马寅燕 高珊
进化树构建	王云凤 高珊
空间结构分析	刘勇
汇总整理和PPT制作	马寅燕 高珊

致谢:

罗老师和助教们的指导
以及班内同学的互相帮助。

谢谢!