Lab Session

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10.21.2020

What we have learned by now

- Neuron Doctrine
  - Neuron, Axon, Dendrite
  - Information flow, Synapse, Convergence and Divergence
  - Wiring optimization principles
- Action potential
  - Membrane potential, Capacitance and Resistance
  - Reversal potential, Resting state and Equilibrium
  - Integrate-and-Fire Models

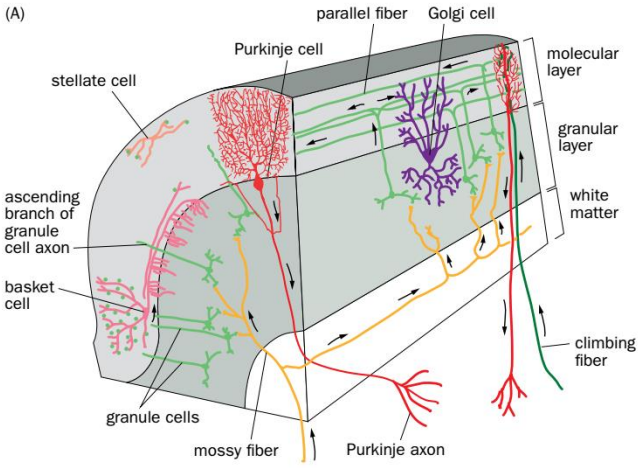
How granule cells sample inputs

Why do we need so many granule cells? What can we say about the number of granule cells N, the number of mossy fiber inputs M, and the convergence of a granule cell K? Perhaps each granule cell is sampling a different combination of mossy fiber inputs. The higher the functional diversity, the more powerful computation downstream circuits (e.g., Purkinje dendrites) could perform, such as classification.

Assume each granule cell can choose K inputs out of all M mossy fibers, the number of possibilities is simply a binomial coefficient $\binom{M}{K}$. Now we ask the following questions.

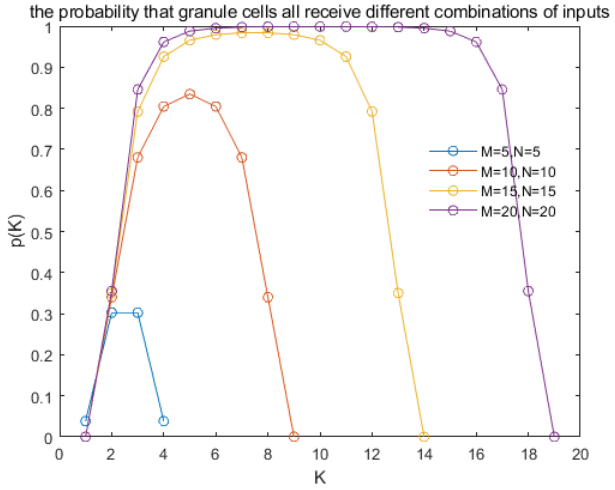
- What is the probability p that granule cells *all* receive *different* combinations of inputs?

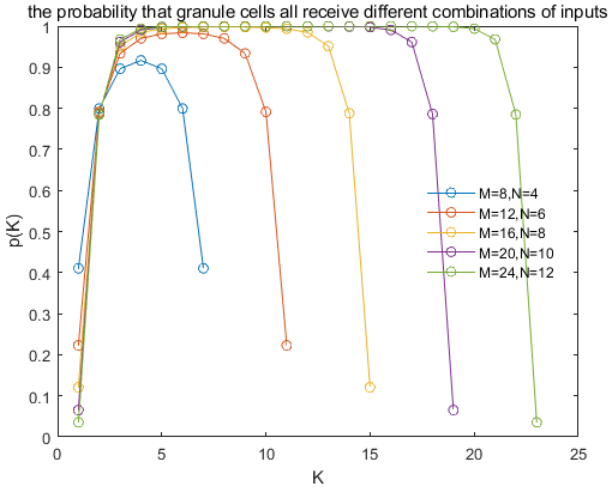
对于给定的 N 和 M, $\text{combination(K)} = \binom{M}{K}$. 所有的 granule cells 得到不同输入组合的概率为 $\text{p(K)}=\frac{A^{N}_{\text{combination(K)}}}{\text{combination(K)}^{N}}$，其中 $A^{N}_{\text{combination(K)}}$ 为排序数(即：将N个granule cells看做不同细胞，当然也可看成相同细胞，则 $\text{p(K)}=\frac{C^{N}_{\text{combination(K)}}}{\text{combination(K)}^{N}/N!}$)，结果一致)。

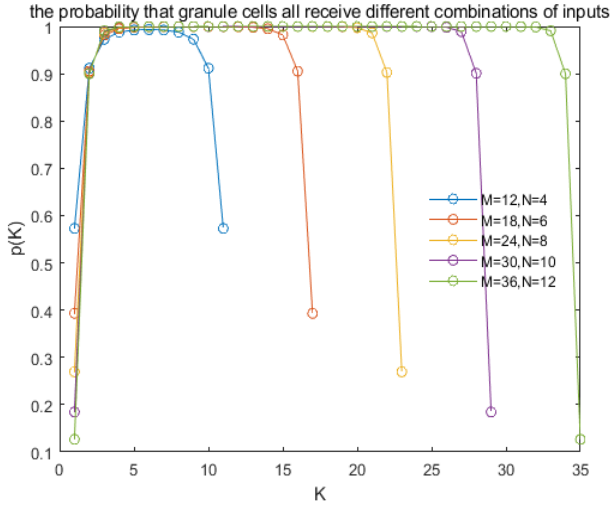


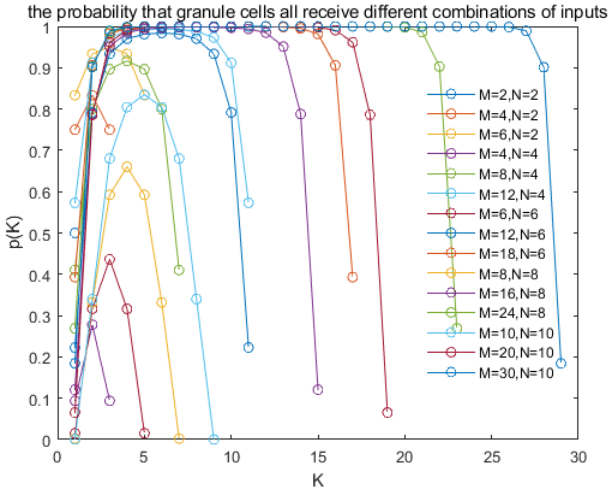
How granule cells sample inputs

- For given N and M, plot p as a function of K, and show when p reaches its maximum.







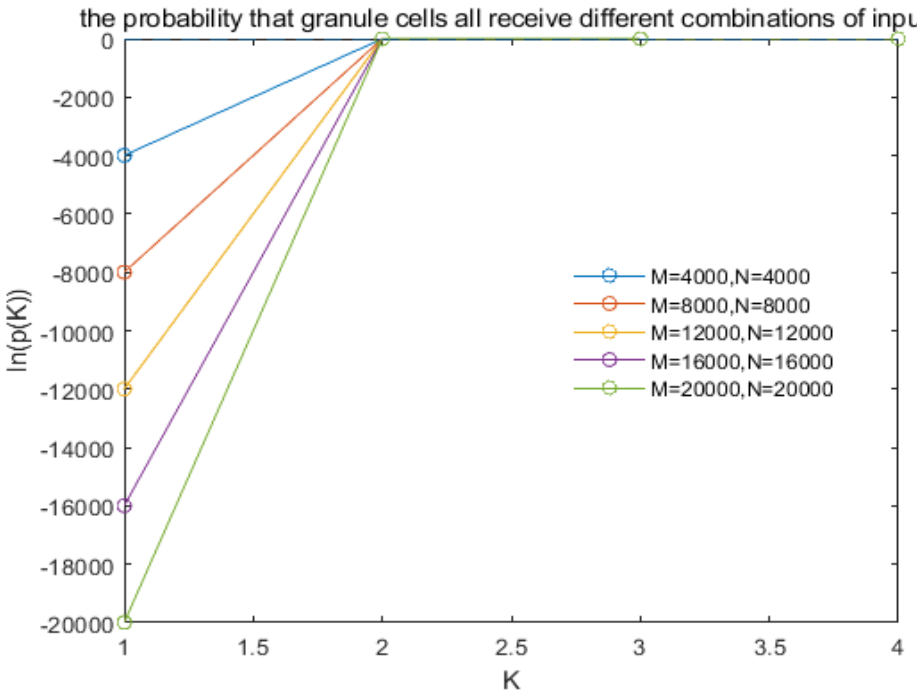


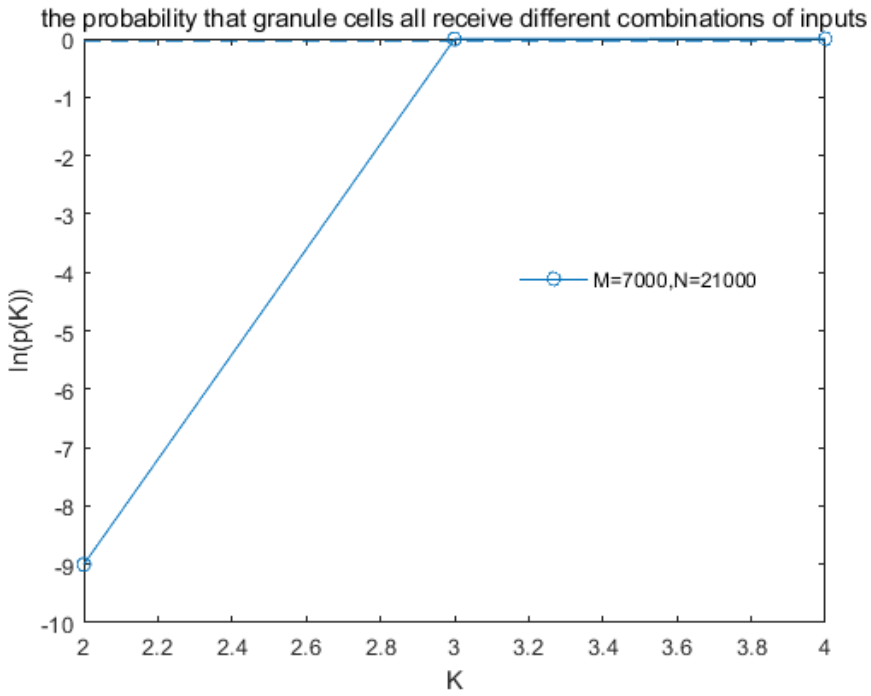
对于较小的N和M，combination(K) = $\binom{M}{K}$.的量级较小，可以进行数值运算。

可以看出，对于不同的N,M，p均在K较小时接近于1。因此，对于较大的N和M，只需运算前几位K即可。

How granule cells sample inputs

- Using $N = 21000$, $M = 7000$, compute K when p approaches 95 percent of its maximum.





K=3时，p已大于0.95.

- Discuss whether it is beneficial to have small K when M is very large.

Visualization of dendritic morphology

Attached you will find morphology data txt files (.swc) of one pyramidal dendrite, one Purkinjie dendrite, and one arbor from larval zebrafish. Use MATLAB or Python to write a simple program:

- Load the data file.

Code:

```
%Load the data file
filename = 'j8_L23pc.CNG.swc.txt';
delimiterIn = ' ';
headerlinesIn = 0;
A = importdata(filename,delimiterIn,headerlinesIn);

segmentindex=A(:,1);
segment_type=A(:,2);
x=A(:,3);
y=A(:,4);
z=A(:,5);
a=[x y z];
segment_diameter=A(:,6);
father_segment_index=A(:,7);
```

Result:

变量 - A

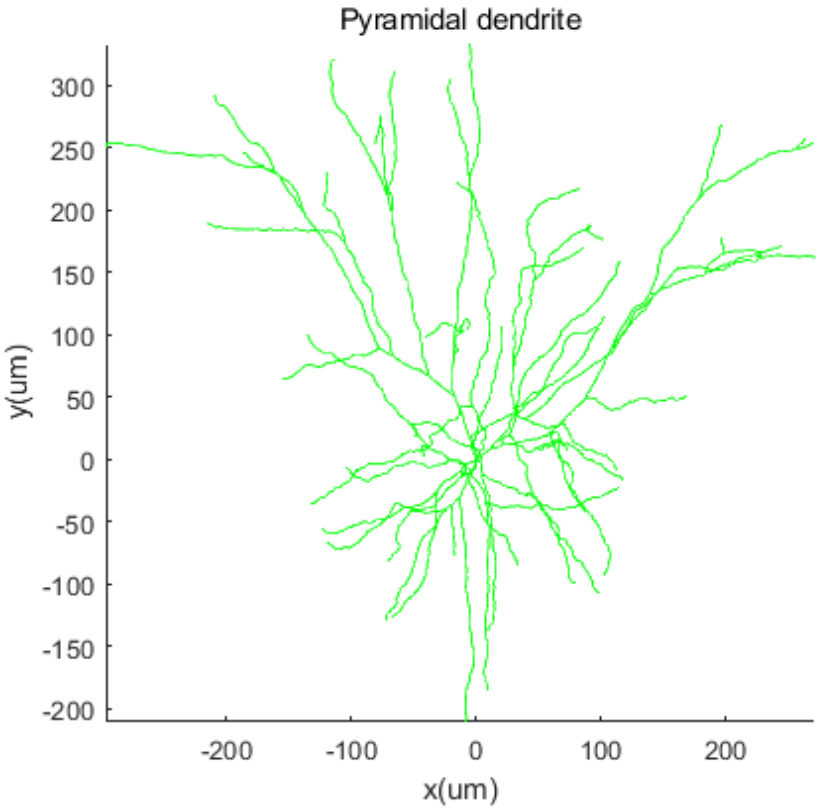
A

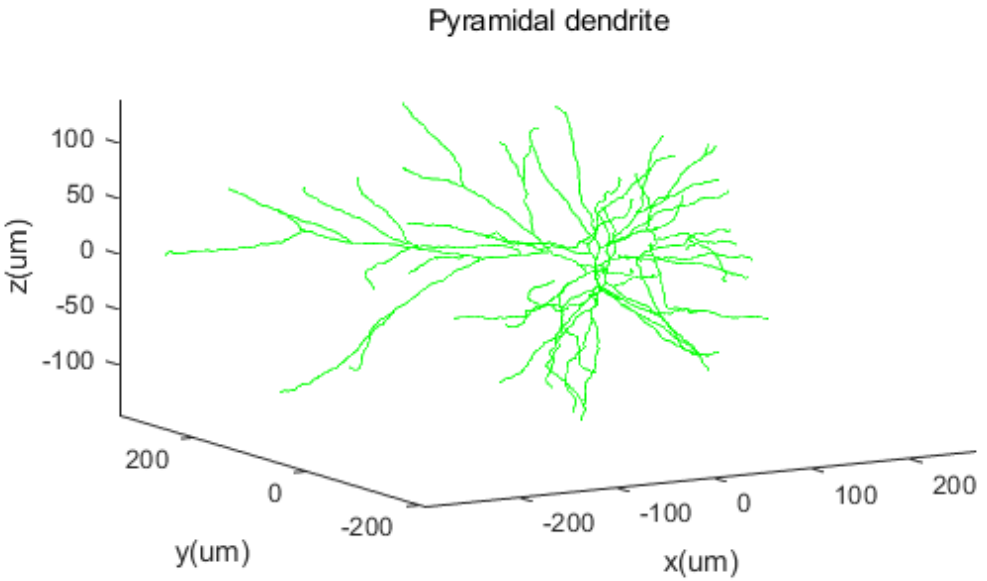
2946x7 double

	1	2	3	4	5	6	7
1	1	1	0	0	0	14.8920	-1
2	2	1	0	0	13.2370	14.8920	1
3	3	3	-1.1000	2.6000	13.2370	1.7500	2
4	4	3	-2	4.1000	13.6370	1.5000	3
5	5	3	-2.8000	7.1000	13.6370	1.5000	4
6	6	3	-3	8.3000	13.6370	1.7500	5
7	7	3	-3.4000	11.6000	12.4370	0.6500	6
8	8	3	-4	14.2000	13.2370	1.2500	7
9	9	3	-4.5000	16.1000	13.6370	1.5000	8
10	10	3	-6.1000	19.4000	11.9370	1.2500	9
11	11	3	-6.7000	21.6000	15.2370	1.2500	10
12	12	3	-7.8000	24.5000	15.4370	0.7500	11
13	13	3	-8.7000	27	15.9370	1.3500	12
14	14	3	-9.2000	28.1000	16.9370	1.2500	13
15	15	3	-9.9000	30.8000	16.9370	1.2500	14
16	16	3	-10.5000	33	16.9370	1.2500	15
17	17	3	-11.6000	37.5000	17.9370	1.1500	16
18	18	3	-12.9000	40.2000	18.2370	1.3500	17
19	19	3	-15.2000	44.2000	18.6370	1.3500	18
20	20	3	-15.9000	46.5000	18.9370	1.2500	19

Visualization of dendritic morphology

- Plot and visualize the neuronal 3D arbor shape.





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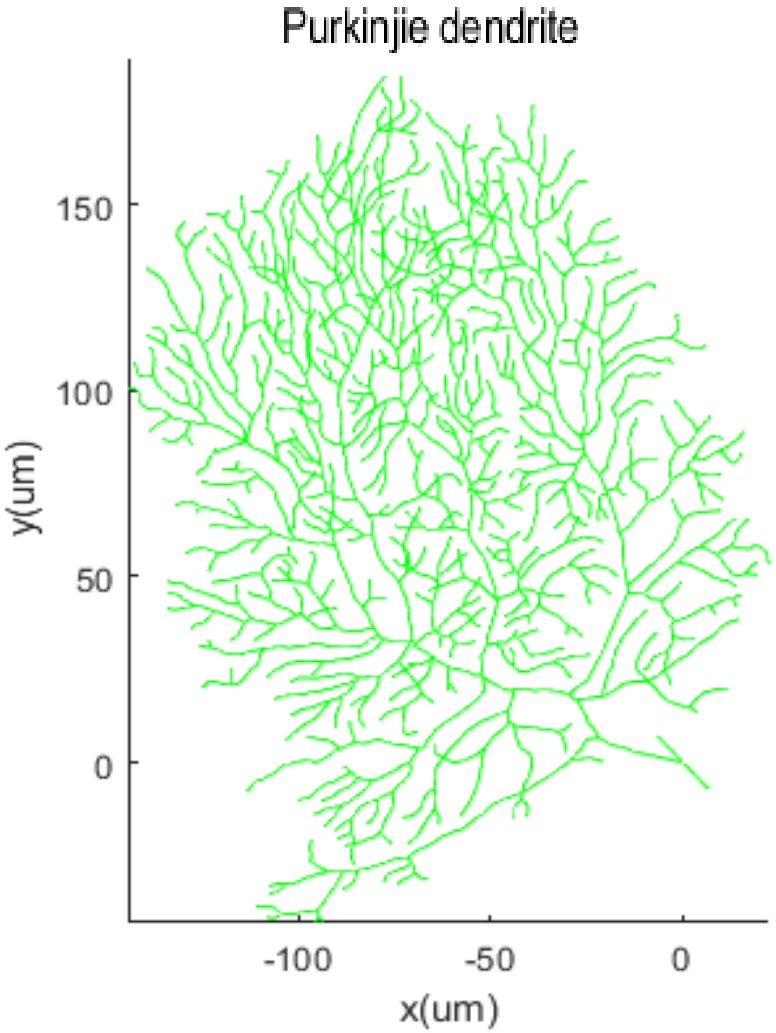

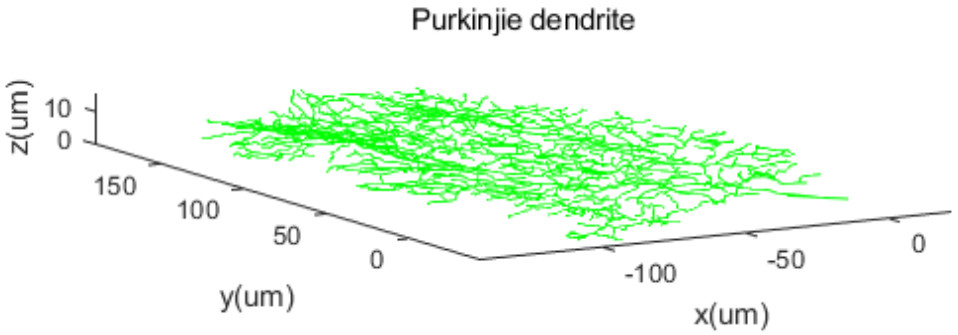

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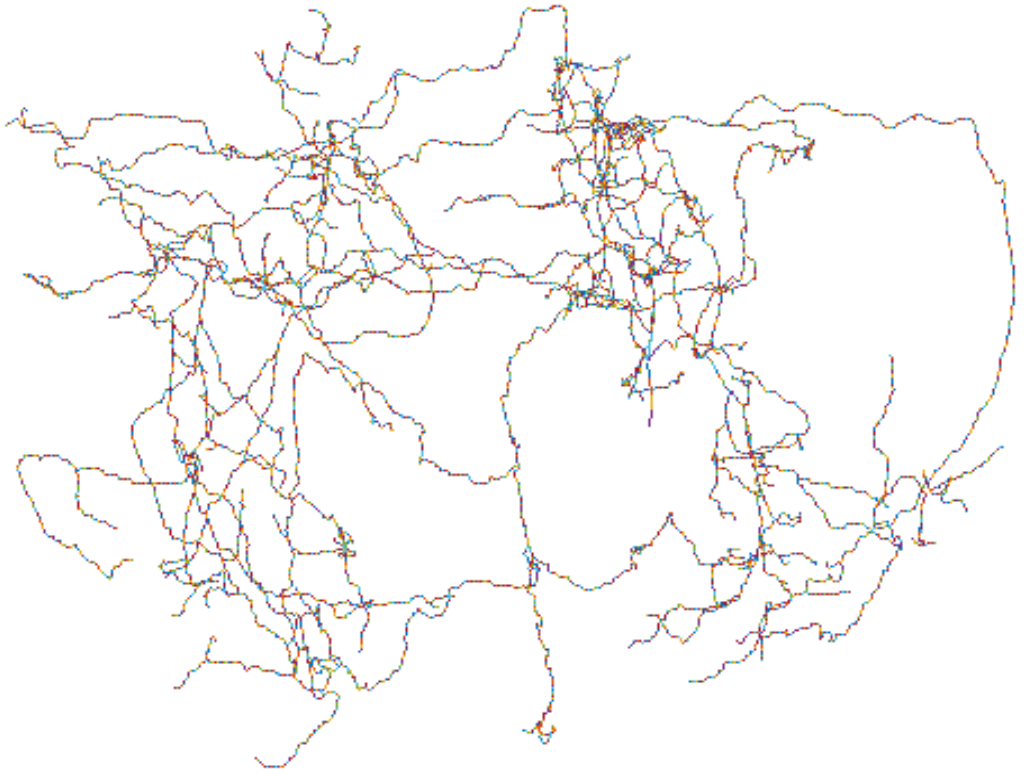
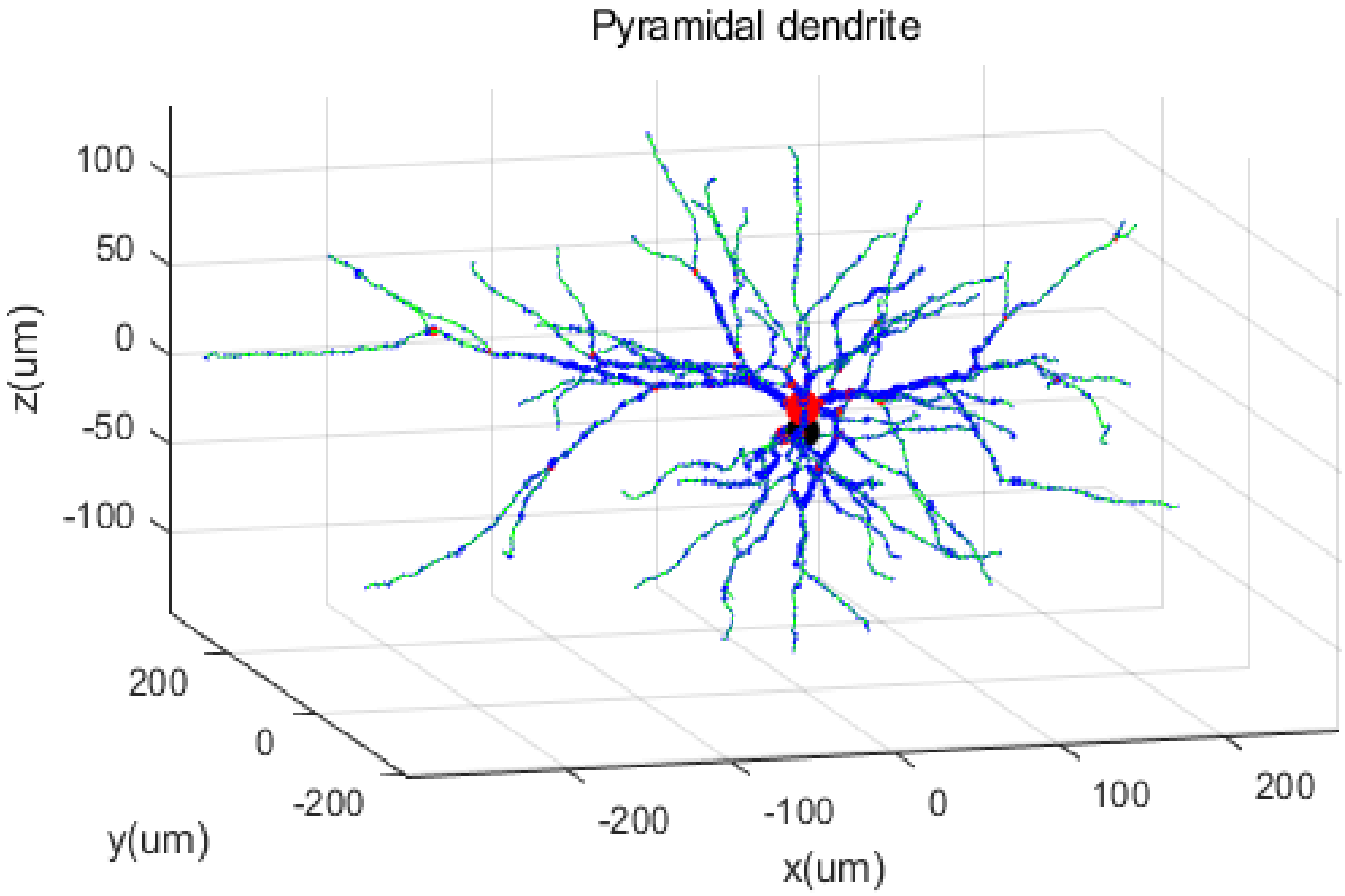


斑马鱼神经分叉点数目为128。

Visualization of dendritic morphology

- Calculate how many branching points on the dendritic arbors.



只需寻找**子节点数目大于等于2**的父节点即为分叉点。

Red: branching points

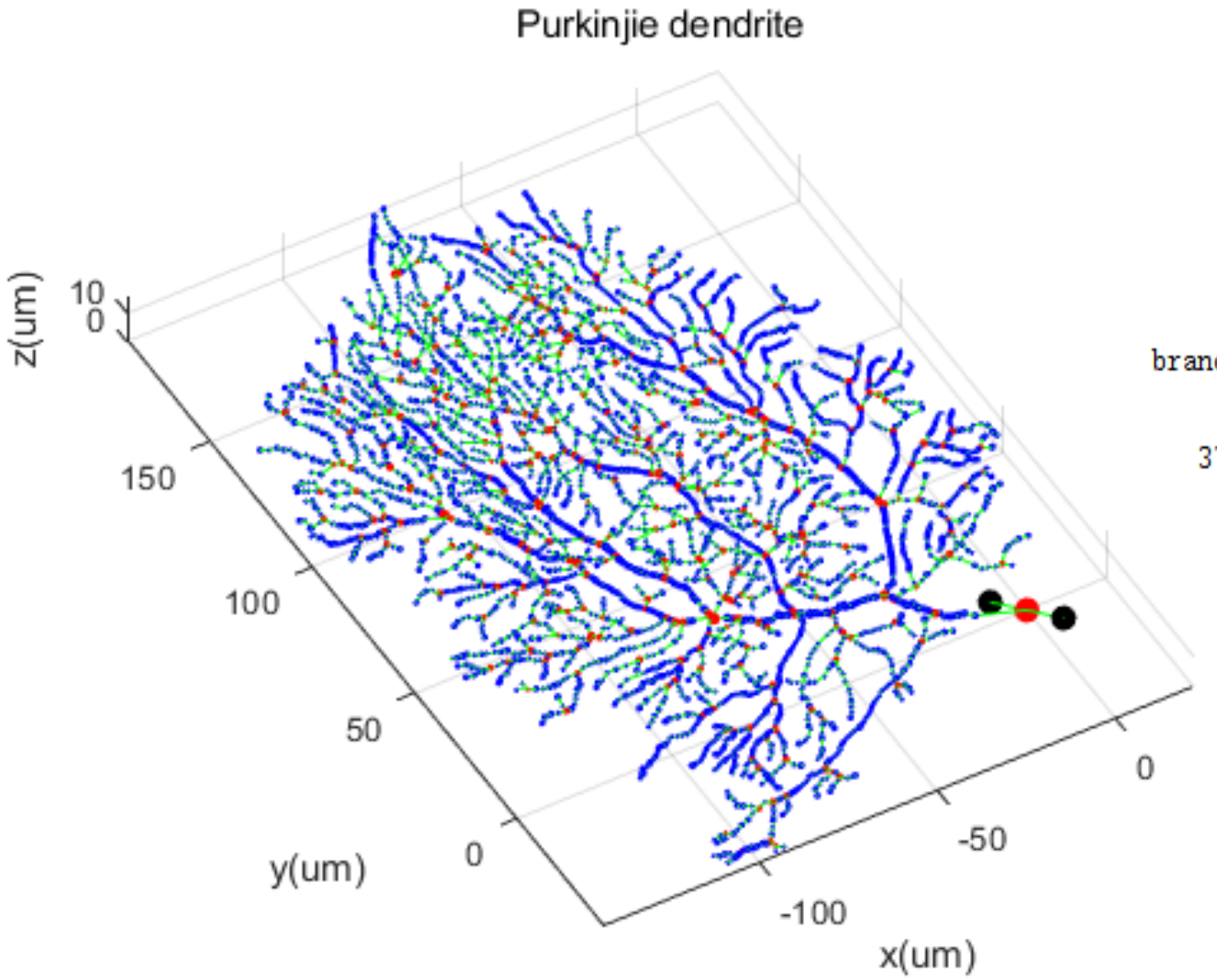
Blue： dendrite

Green： line

```
branching_points_num =

    51
```

Visualization of dendritic morphology

- Calculate how many branching points on the dendritic arbors.

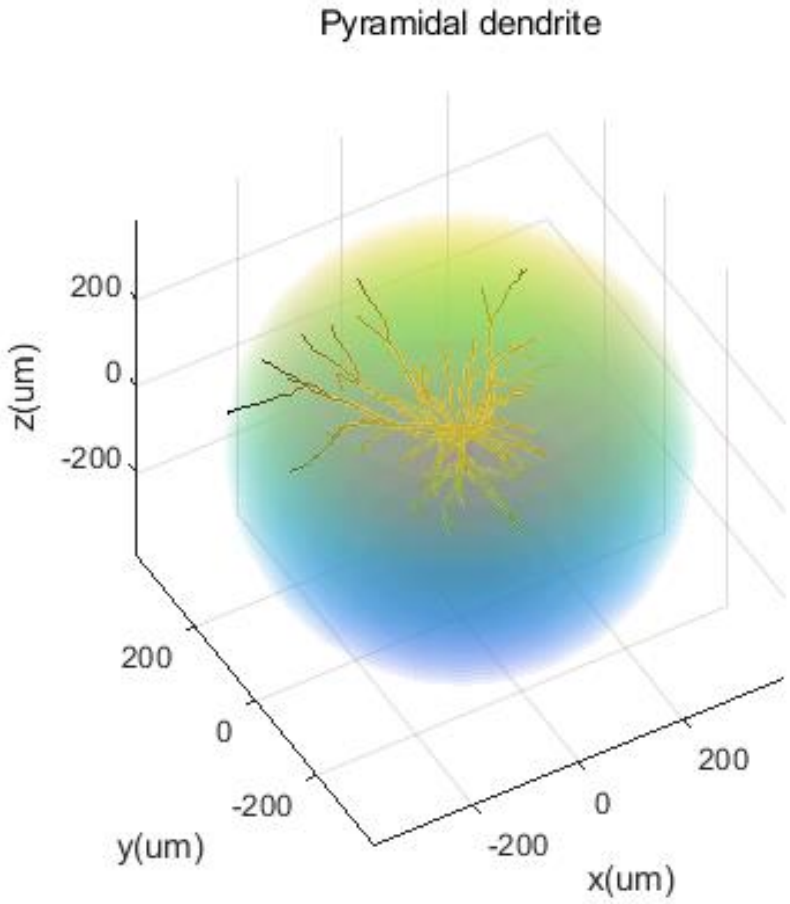


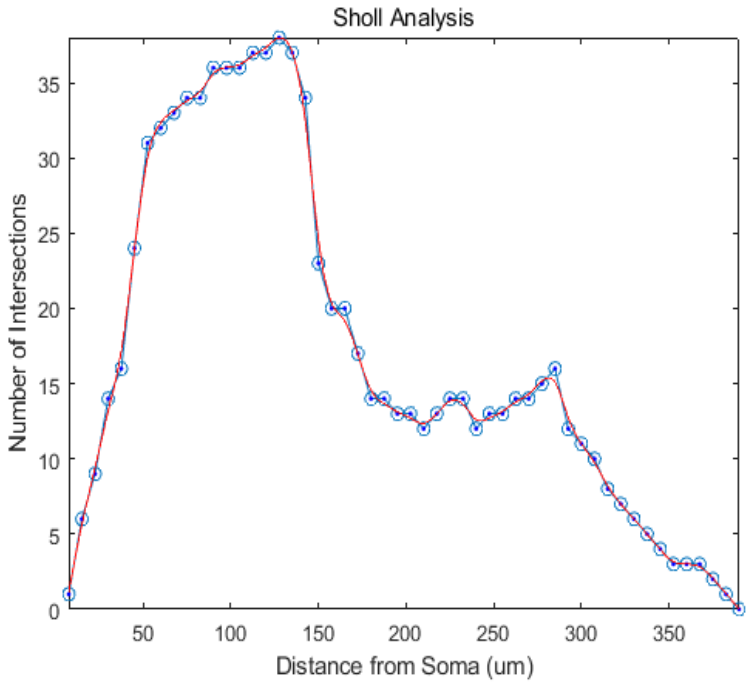

```
branching_points_num =

   379
```

Visualization of dendritic morphology

- Perform a Sholl plot. Center on the cell body and draw spheres, and plot the number of intersections between sphere and dendrites as a function of sphere radius.

比较每个节点到胞体的距离即可得到intersections的数目。





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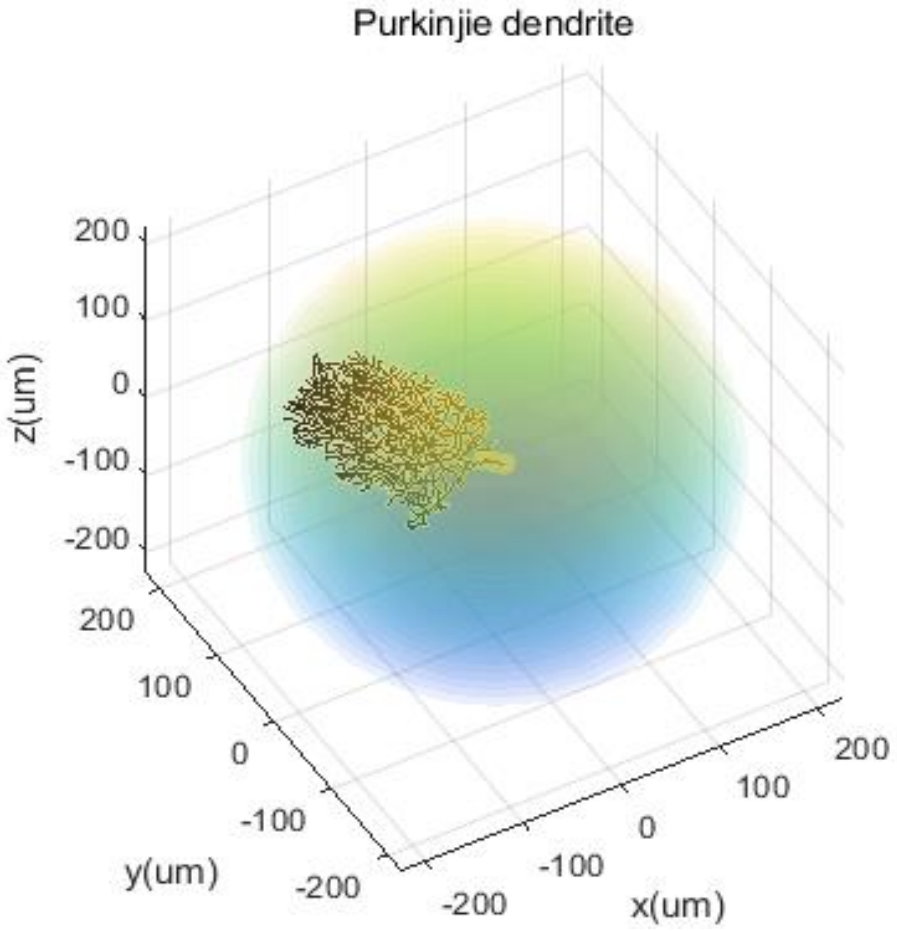

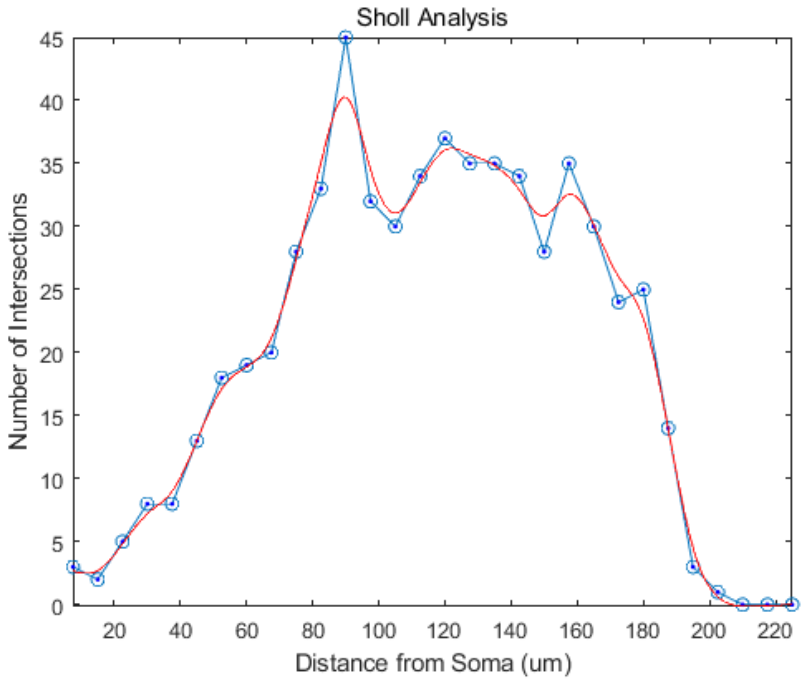

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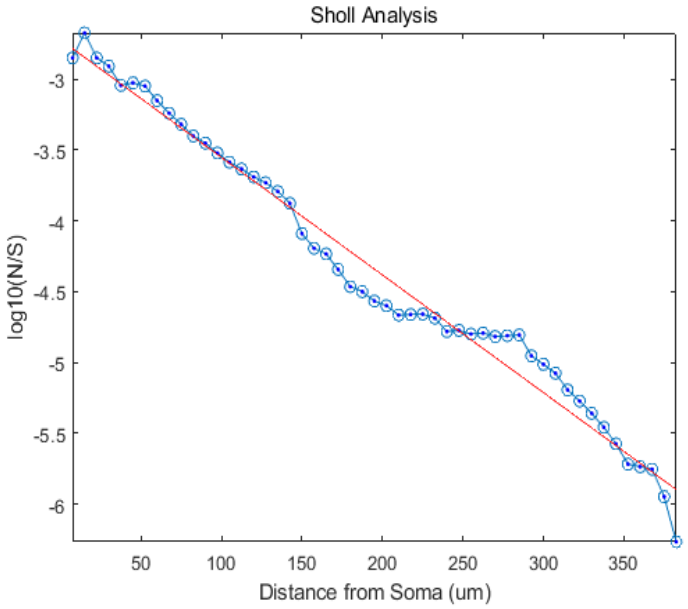



```
Linear model Poly1:
f(x) = p1*x + p2
Coefficients (with 95% confidence bounds):
  p1 =   -0.008303  (-0.008653, -0.007953)
  p2 =       -2.72  (-2.799, -2.642)
```

Semi-Log Method [edit]

Somewhat more complicated than the Linear Method, the Semi-Log Method begins by calculating the function Y(r) = N/S where N is the number of dendrite crossings for a circle of radius r, and S is the area of that same circle. The base 10 logarithm is taken of this function, and a first order linear regression, linear fit, is performed on the resulting data set, that is

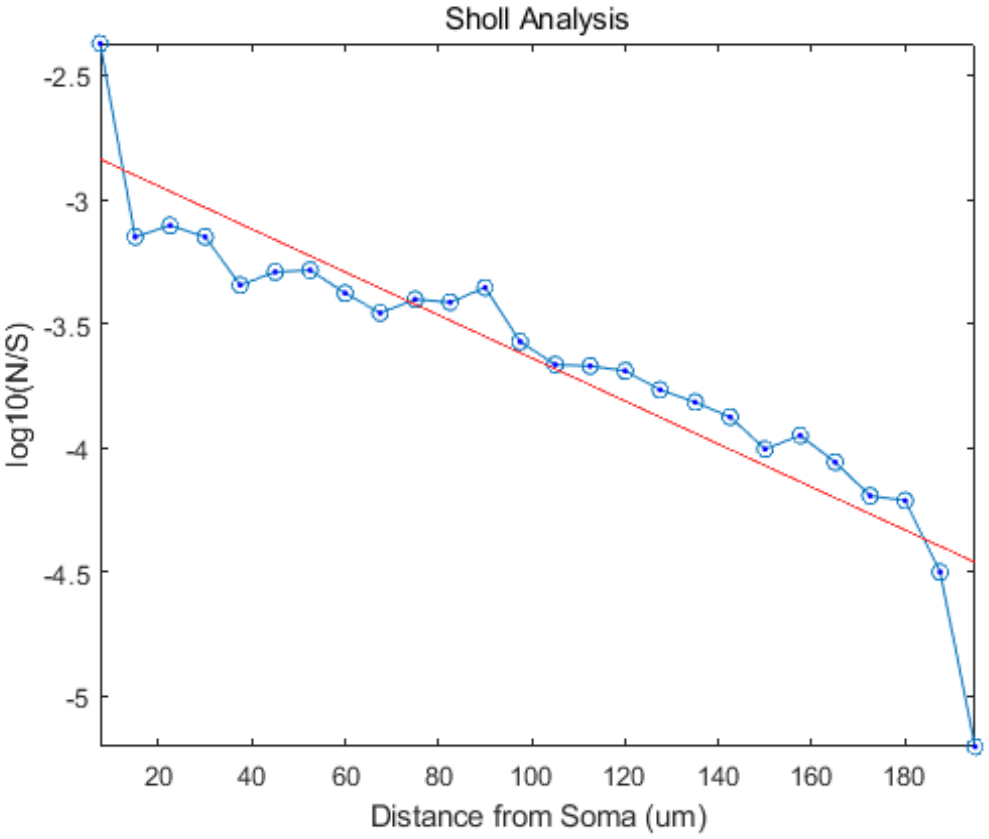
$$\log_{10}\left(\frac{N}{S}\right) = -k \cdot r + m.$$

where **k** is Sholl's Regression Coefficient.[1]

Sholl's Regression Coefficient is the measure of the change in density of dendrites as a function of distance from the cell body.[5] This method has been shown to have good discrimination value between various neuron types, and even similar types in different regions of the body.

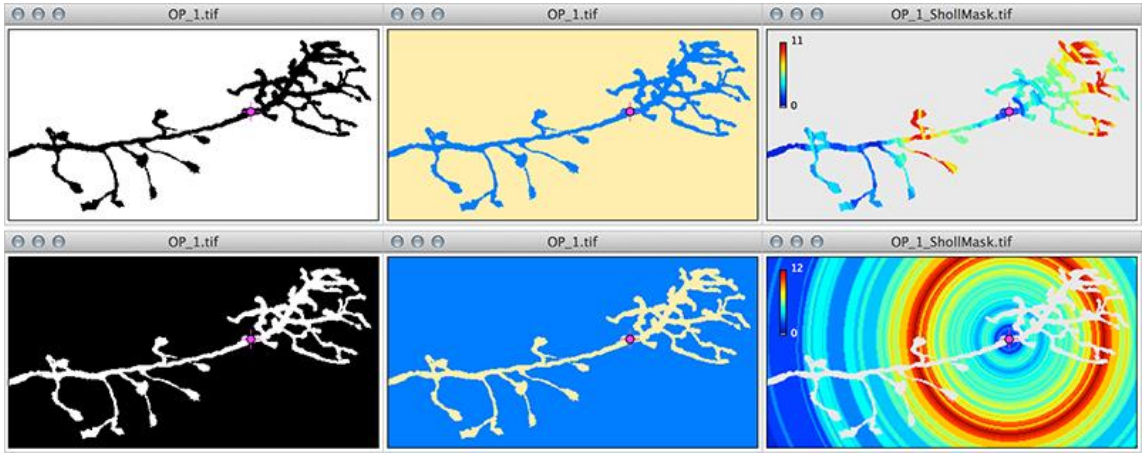
Visualization of dendritic morphology

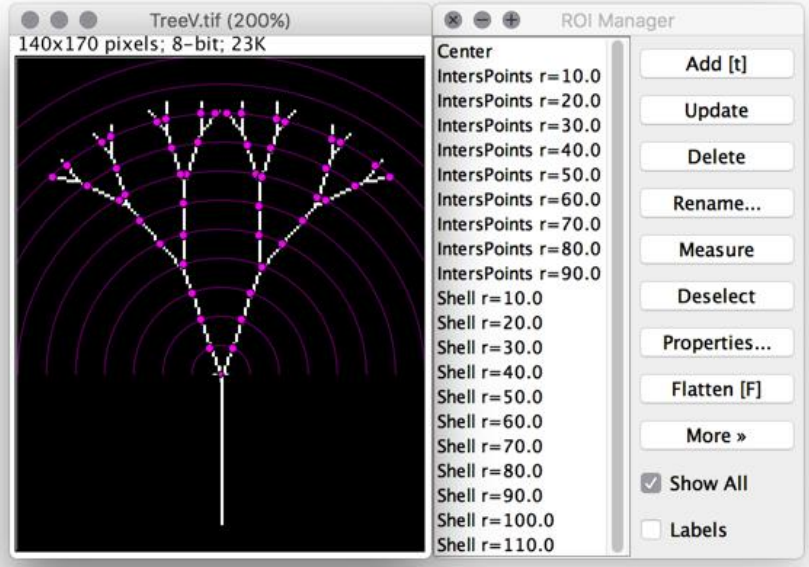
- Perform a Sholl plot. Center on the cell body and draw spheres, and plot the number of intersections between sphere and dendrites as a function of sphere radius.




```
Linear model Poly1:
f(x) = p1*x + p2
Coefficients (with 95% confidence bounds):
  p1 =   -0.008654  (-0.01024, -0.007071)
  p2 =      -2.773  (-2.956, -2.589)
```

Visualization of dendritic morphology





https://imagej.net/Sholl_Analysis#Sholl_Plots

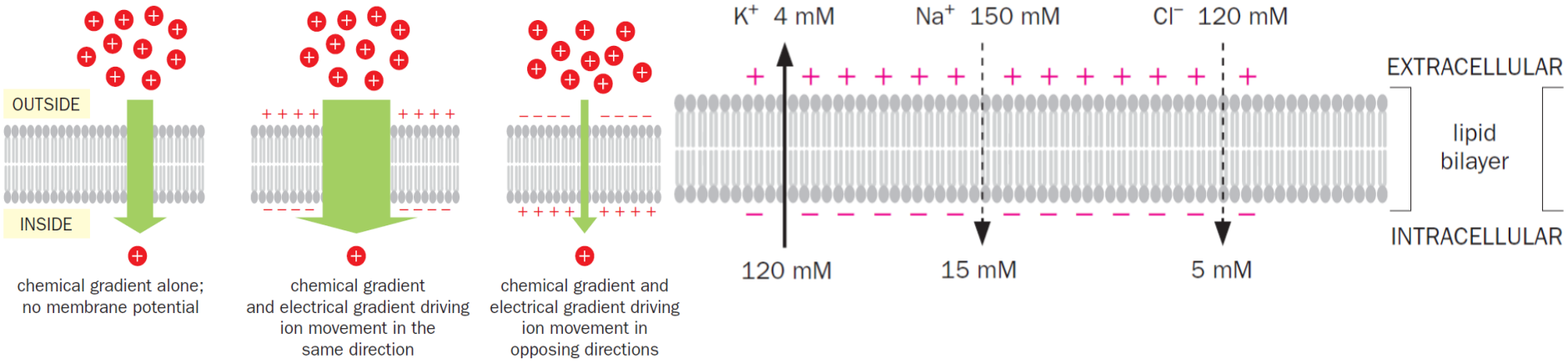
Derivation of the Goldman-Hodgkin-Katz formula for membrane potential

The reversal potential we discussed in the class only take into account one type of ion. However, some channels are not quite selective, and we need to combine the current flow from multiple ions, and the result is the Goldman-Hodgkin-Katz formula for membrane potential. I will write down the equation here, and it is your homework to provide the derivation of this formula.

$$V_m = \frac{k_B T}{e} \ln \left(\frac{\sum_{i=1}^{N} P_{M_i^+} [M_i^+]_{out} + \sum_{j=1}^{N} P_{A_j^-} [A_j^-]_{in}}{\sum_{i=1}^{N} P_{M_i^+} [M_i^+]_{in} + \sum_{j=1}^{N} P_{A_j^-} [A_j^-]_{out}} \right) . \qquad (1)$$

Here P denotes the permeability of a given ion.

Derivation of the Goldman-Hodgkin-Katz formula for membrane potential



膜电位达到稳态时，离子跨膜扩散形成的静电流应为0，且对于每种离子，其扩散速率（单位电流强度）正比于离子浓度、渗透能力（permeability）和克服静电势的概率（Boltzman distribution）,故得到以下所有一价离子的平衡方程：

$$\sum_{i=1}^{N} P_{M_i^+}[M_i^+]_{in} + \sum_{i=1}^{N} P_{A_j^-}[A_j^-]_{out}$$

$$= \exp(-Ee/kT) \left(\sum_{i=1}^{N} P_{M_i^+}[M_i^+]_{out} + \sum_{i=1}^{N} P_{A_j^-}[A_j^-]_{in} \right)$$

移项静息电位：

$$E_m = \frac{k_B T}{e} \ln \left(\frac{\sum_{i=1}^{N} P_{M_i^+}[M_i^+]_{out} + \sum_{i=1}^{N} P_{A_j^-}[A_j^-]_{in}}{\sum_{i=1}^{N} P_{M_i^+}[M_i^+]_{in} + \sum_{i=1}^{N} P_{A_j^-}[A_j^-]_{out}} \right).$$

Integrate and Fre neuron

An integrate and fire neuron has a subthreshold membrane potential that obeys the equation

$$C\frac{dV}{dt} = -\frac{V}{R} + I(t) \tag{2}$$

Once the voltage crosses threshold, the neuron fires a spike and V is reset to 0, as discussed in the class.

Consider the input current

$$I(t) = Q\sum_{k=-\infty}^{\infty} \delta(t - kT) \tag{3}$$

where a charge Q crosses the membrane periodically, and $\delta(x)$ is the Dirac delta function.

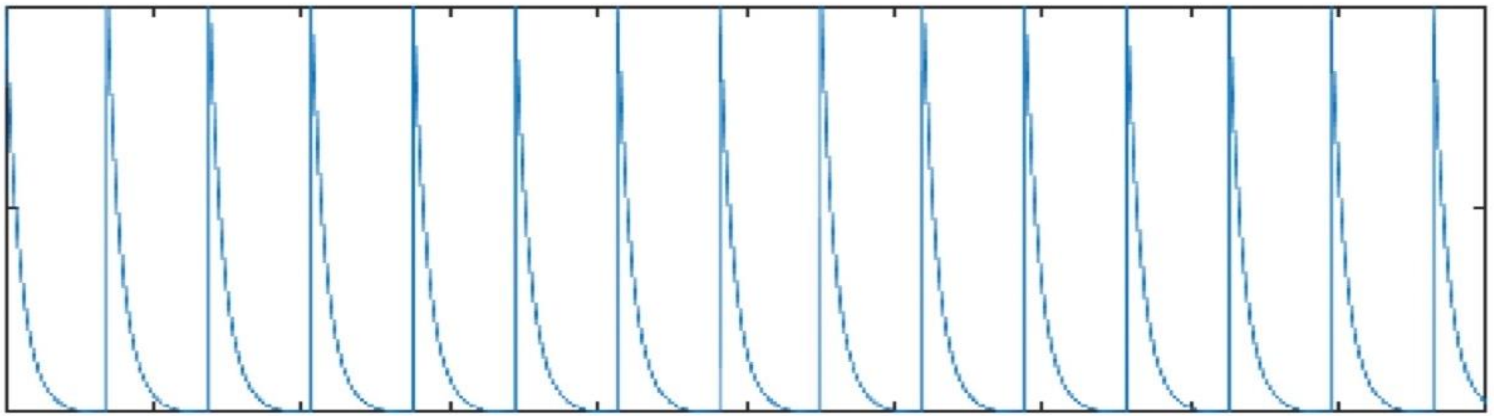
- Derive the subthreshold membrane potential as a function of time for this input current. Describe the transient and steady state behavior of the potential. Illustrate the result by qualitative or (even better) numerically quantitative graphs.

Integrate and Fre neuron

$$C\frac{dV}{dt} = -\frac{V}{R}$$

$$C(V_+ - V_-) = Q$$

$$V(t) = \frac{Q}{C}\frac{1}{1 - e^{-\frac{T}{CR}}} e^{-\frac{t-nT}{\tau_a}} \qquad t \in [nT, (n+1)T]$$



Science is “ the art of the soluble”.

——Peter Medawar

To be continued.....