

Exercise session, week 12

Course: *Systèmes dynamiques en biologie* (BIO-341)

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```
In [1]: # import important libraries
import numpy as np
import matplotlib
import matplotlib.pyplot as plt
from IPython.display import set_matplotlib_formats
from scipy.integrate import odeint

# set_matplotlib_formats("png", "pdf")
matplotlib.rc("image", cmap="RdBu")
import matplotlib.animation as animation
from random import random
from time import time
```

A. Organization of the circadian oscillator network in the brain

In mammals, circadian timing is regulated by the master clock, which is composed of about 20000 neurons located in the suprachiasmatic nucleus (SCN) in the hypothalamus. The neurons in the SCN are synchronized with each other, in part, by neurotransmitters that are secreted by the neurons. Here, we are interested in how different neuron connectivities affect collective synchronization and oscillatory behavior. For simplicity, we will consider a theoretical model of the SCN in which coupled oscillators are arranged in a 2-dimensional space (grid). We can construct a symmetric adjacency matrix (coupling matrix) $\mathbf{A}$ where $\mathbf{A}_{ij} = \mathbf{A}_{ji}$ specifies the coupling between oscillator i and oscillator j . Here, we consider the simplest case where $\mathbf{A}_{ij}$ is either 0 or 1. This coupling is modulated by a strength K .

For each neuron i , $\dot{\theta}_i = f_i + K \sum_{j=1}^N \mathbf{A}_{ij} \sin(\theta_j - \theta_i)$.

We provide you with two functions:

- heatmap: plot a $n \times n$ grid ($N := n^2$ being the number of neurons), which represents the SCN. Each cell shows the value contained in the matrix *datagrid*. The values are plotted from bottom left to top right, row by row.
- value_to_size: create the grid on which the oscillators are. This function is called by heatmap.

```

In [2]: # create a grid on which the oscillators are

def value_to_size(val, size_min, size_max, size_scale):
    val = abs(val) # to handle negative numbers
    val_position = (val - size_min) * 0.99 / (
        size_max - size_min
    ) + 0.01 # position of value in the input range, relative to the length
    return val_position * size_scale

def heatmap(datagrid, marker, ax):
    x = list(range(datagrid.shape[1]))
    y = list(range(datagrid.shape[0]))

    size_min, size_max = 0, 1
    size_scale = 500

    # dot the scatter + 2 extra invisible points to normalize colors
    scat = ax.scatter(
        x=x * len(y) + [-100, -100],
        y=[v for v in y for p in x] + [-100, -100],
        marker=marker,
        s=[value_to_size(v, size_min, size_max, size_scale) for v in datagrid
          + [1, 1],
        c=[v for v in datagrid.flatten()] + [-1, 1],
        cmap="RdBu",
    )

    ax.set_xticks(x)
    ax.set_xticklabels(x)
    ax.set_yticks(y)
    ax.set_yticklabels(y)

    ax.grid(False, "major")
    ax.grid(True, "minor")

    ax.set_xticks([t + 0.5 for t in ax.get_xticks()], minor=True)
    ax.set_yticks([t + 0.5 for t in ax.get_yticks()], minor=True)

    ax.set_xlim([-0.5, max(x) + 0.5])
    ax.set_ylim([-0.5, max(y) + 0.5])
    ax.set_facecolor("#F1F1F1")

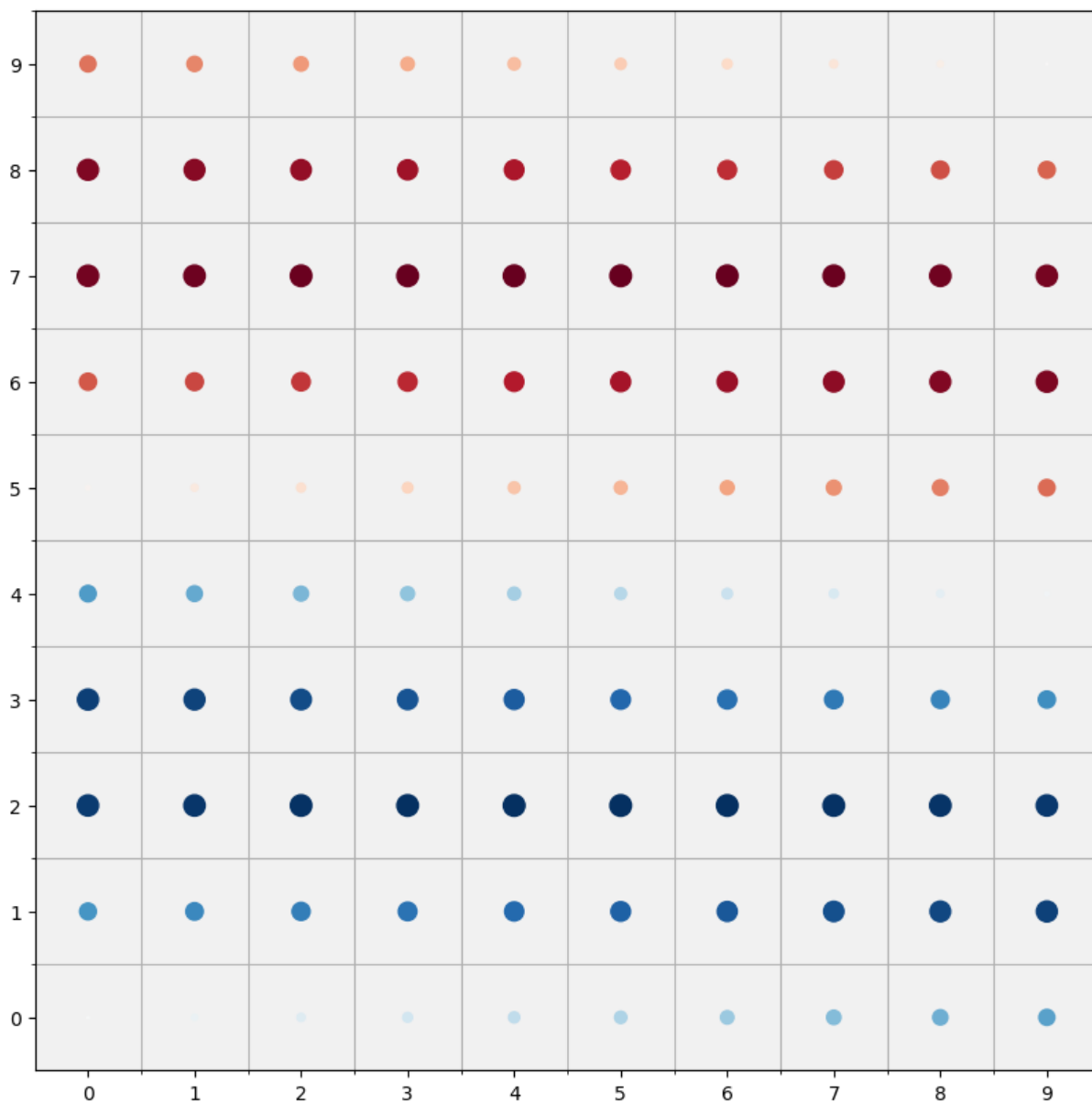
```

Below is an example of how to use the functions to plot the phase of each neuron in each cell of the grid:

```
In [3]: # create 100 cells (10*10 grid)
N = 100
n = int(N**0.5)

# create a vector of increasing phases to check the order of the oscillators
l_x0 = np.linspace(0, 2 * np.pi, N)
print(l_x0.shape)
# reshape l_x0 to match the grid
X = np.reshape(l_x0, (n, n))
print(X.shape)
# plot the oscillators
datagrid = np.sin(X)
fig, ax = plt.subplots(figsize=(X.shape[0], X.shape[1]))
heatmap(datagrid, marker=".", ax=ax)
plt.show()
```

```
(100,)
(10, 10)
```



Question 1:

Assume that every neuron is connected to its nearest neighbours in the grid: for example, a neuron in position (i, j) will be connected to the neurons at $(i - 1, j)$, $(i + 1, j)$, $(i, j - 1)$ and $(i, j + 1)$. Assume also that the neuron is connected to its second nearest neighbours: $(i - 1, j - 1)$, $(i - 1, j + 1)$, $(i + 1, j - 1)$, $(i + 1, j + 1)$.

Visualize the circadian oscillations of neurons at different times using the provided function heatmap and using subplots.

Hint : Initialize the parameters of a population of N neurons ($N \sim 100\text{--}1000$ cells) with varying intrinsic periods of about 24 hours. For instance, you can modify the period of a neuron i by drawing f_i from a normal distribution with $\mu = 2\pi/24$ and σ equal to 5% of the mean (you may have to play with σ to obtain synchronization). Assign coordinates to each cell in a 2D grid, e.g. with x and y coordinates in a rectangle (the real SCN has an 'egg' shape). Choose $K = 0.03$.

```
In [4]: def model(
        l_theta, t, l_f, K, A
    ): # l_theta: list of initial phase of the N neurons, t = time (needed for
        # l_f: intrinsic frequencies of the neurons, K: coupling strength, A: in

        # compute interaction matrix
        INT = np.zeros((len(l_theta), len(l_theta)))
        for i, theta_i in enumerate(l_theta):
            for j, theta_j in enumerate(l_theta):
                INT[i, j] = np.sin(theta_j - theta_i)

        # multiply by the interaction matrix
        NINT = np.multiply(INT, A)

        # simulate the system with the new set of interaction
        return np.array(
            [f + K * np.sum(NINT[i, :]) for i, (theta, f) in enumerate(zip(l_theta, l_f))])
```

```

In [5]: # Defining some interaction matrices
def A_alltoall(N, p=1):
    A = np.zeros((N, N))
    for i in range(A.shape[0]):
        for j in range(i, A.shape[1]):
            A[i, j] = 1 if random() < p else 0
            A[j, i] = A[i, j]
    return A

def A_NN(N):
    # Nearest Neighbours

    A = np.zeros((N, N))
    n = int(np.sqrt(N))
    neuron_index = np.arange(N)
    NI = np.reshape(neuron_index, (n, n))

    for i in range(n): # row number
        for j in range(n): # column number
            if i < n - 1:
                A[NI[i, j]][NI[i + 1, j]] = 1

            if i > 0:
                A[NI[i, j]][NI[i - 1, j]] = 1

            if j < n - 1:
                A[NI[i, j]][NI[i, j + 1]] = 1

            if j > 0:
                A[NI[i, j]][NI[i, j - 1]] = 1

            A[NI[i, j]][NI[i, j]] = 1

    return A

def A_2NN(N):
    # First and second Nearest Neighbours

    A = A_NN(N)
    n = int(np.sqrt(N))
    neuron_index = np.arange(N)
    NI = np.reshape(neuron_index, (n, n))

    for i in range(n): # row number
        for j in range(n): # column number
            # second nearest neighbours
            if i < n - 1 and j < n - 1:
                A[NI[i, j]][NI[i + 1, j + 1]] = 1

            if i < n - 1 and j > 0:
                A[NI[i, j]][NI[i + 1, j - 1]] = 1
            if i > 0 and j < n - 1:
                A[NI[i, j]][NI[i - 1, j + 1]] = 1

```

```

        if i > 0 and j > 0:
            A[NI[i, j]][NI[i - 1, j - 1]] = 1

        A[NI[i, j]][NI[i, j]] = 1

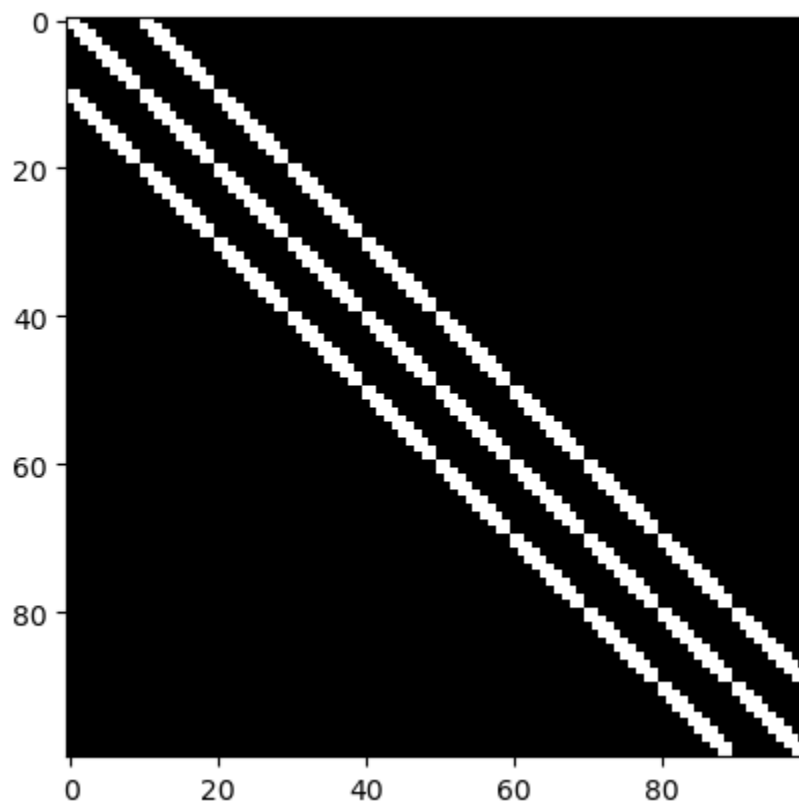
    return A

A1 = A_NN(N)
A2 = A_2NN(N)

plt.imshow(A2, cmap="gray")

```

Out[5]: <matplotlib.image.AxesImage at 0x10e8e3950>



```

In [6]: def order(l_angles):
        return np.mean([np.exp(1j * theta) for theta in l_angles])

```

```

In [7]: # create a vector of intrinsic frequencies
mu = 2 * np.pi / 24
sigma = 0.1 * mu
l_f = np.random.randn(N) * sigma + mu

# define time domain
dt = 0.25 # fixed
nsteps = 1000
T = dt * nsteps

tspan = np.linspace(0, T, nsteps)

# define coupling strength
K = 0.03

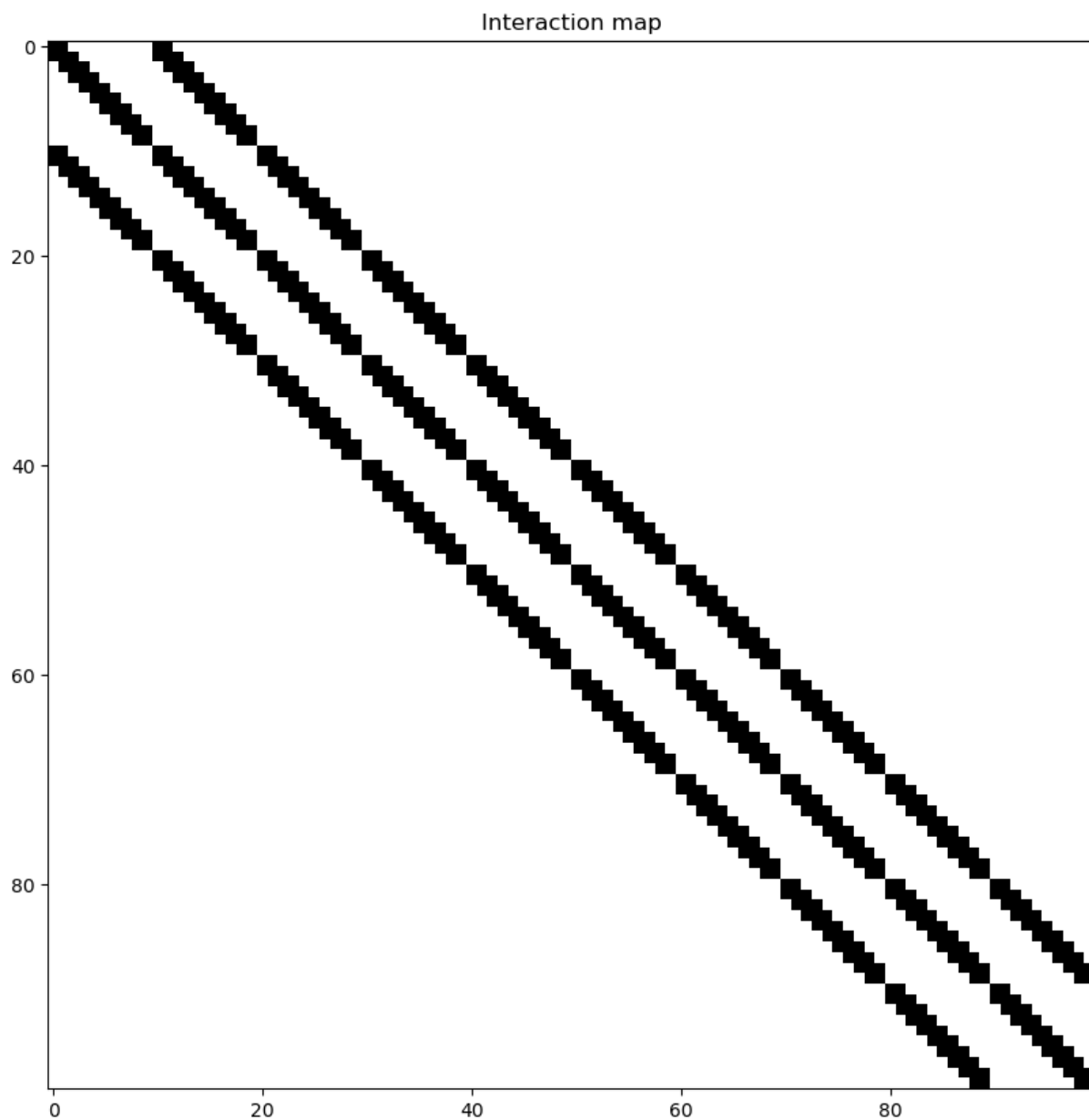
# define interaction matrix
A = A_2NN(N)

# plot the interaction matrix
fig, ax = plt.subplots(figsize=(10, 10))
ax.imshow(A, cmap="Greys")
ax.set_title("Interaction map")

# simulate cells, crucial step!
X = odeint(model, l_x0, tspan, args=(l_f, K, A))
print(X.shape)
# reshape X to match the interaction grid
X = np.reshape(X, (X.shape[0], n, n))

(1000, 100)

```



```
In [8]: X.shape
```

```
Out[8]: (1000, 10, 10)
```

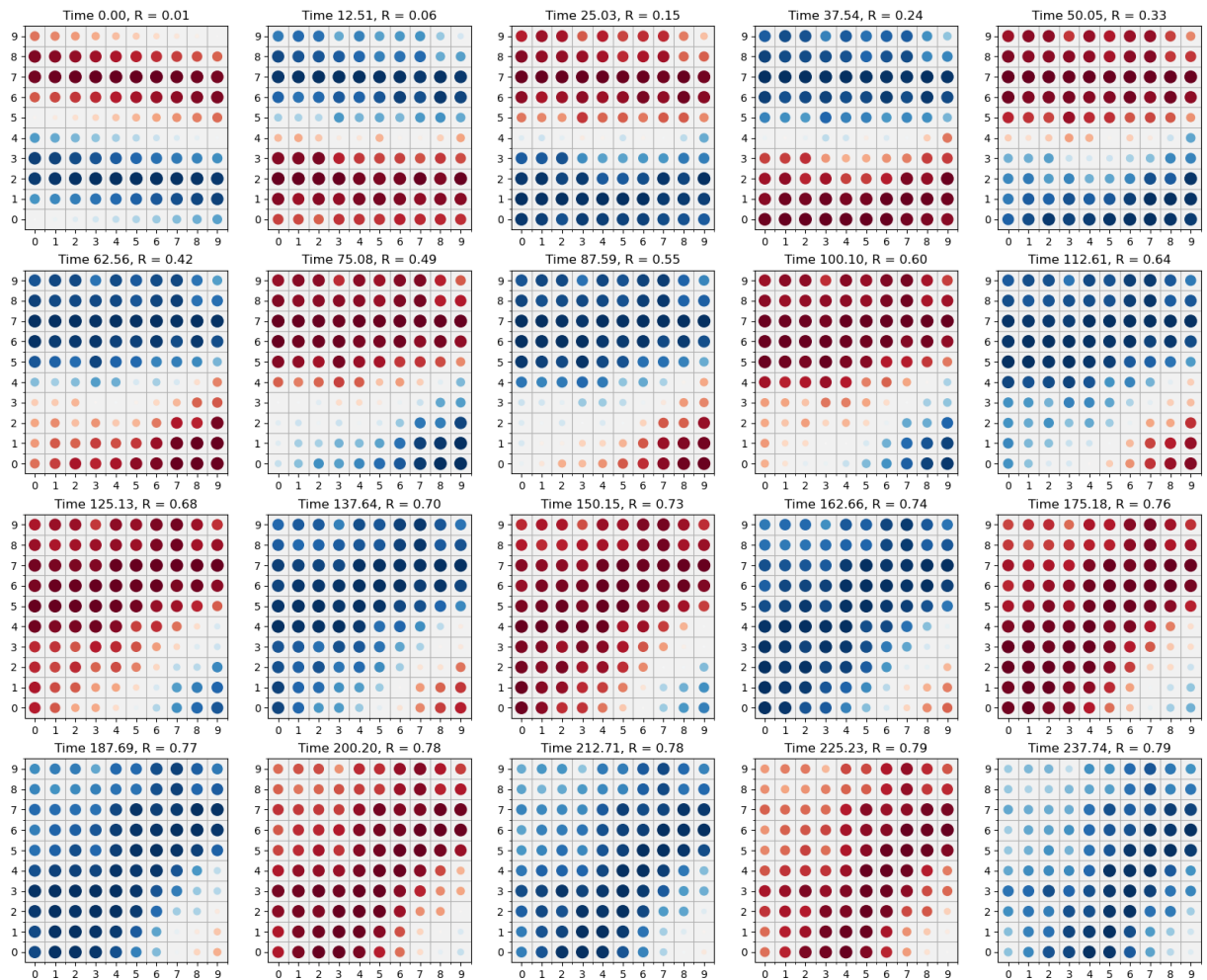


```
In [9]: fig, axs = plt.subplots(4, 5, figsize=(20, 16))
axs = axs.flatten()

i_show = np.arange(0, nsteps, int(nsteps / 20))

# looping over the time steps to plot the oscillators
for ax, i in zip(axs, i_show):
    # X represents the phases therefore we need to take the sin of it to plot
    datagrid = np.sin(X[i, :])
    heatmap(datagrid, marker=".", ax=ax)
    # here it is crucial the part with abs(order(X[i, :]))
    # it takes the average of the thetas around the circle and then takes the
    ax.set_title("Time {0:.2f}, R = {1:.2f}".format(tspan[i], abs(order(X[i, :]))))

plt.show()
```



Question 2

Do the same plots as for Question 1 but for an all-to-all interaction matrix: $A_{ij} = 1$ for all i, j . Set $K = 0.001$.

How does the space-time synchronization dynamics change with respect to the previous case?

```

In [10]: # create a vector of intrinsic frequencies
mu = 2 * np.pi / 24
sigma = 0.1 * mu
l_f = np.random.randn(N) * sigma + mu

# define time domain
dt = 0.25 # fixed
nsteps = 1000
T = dt * nsteps

tspan = np.linspace(0, T, nsteps)

# define coupling strength
K = 0.001 #

# define interaction matrix
A = A_alltoall(N)

# fig, ax = plt.subplots(figsize=(10, 10))
# ax.imshow(A, cmap='Greys')
# ax.set_title("Interaction map")

# simulate cells
X = odeint(model, l_x0, tspan, args=(l_f, K, A))

# reshape X to match the interaction grid
X = np.reshape(X, (X.shape[0], n, n))

```

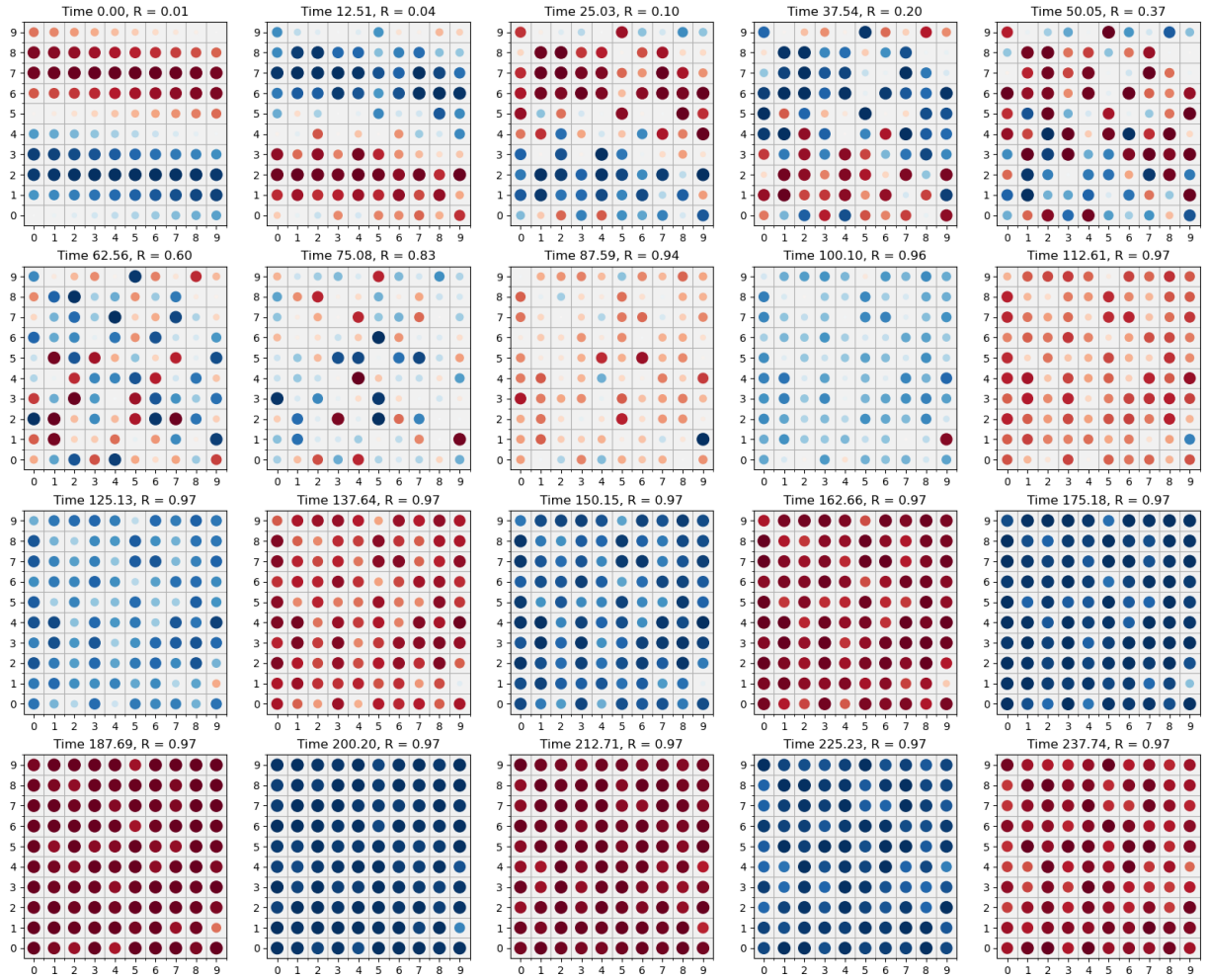
```

In [11]: fig, axs = plt.subplots(4, 5, figsize=(20, 16))
axs = axs.flatten()

i_show = np.arange(0, nsteps, int(nsteps / 20))

for ax, i in zip(axs, i_show):
    datagrid = np.sin(X[i, :])
    heatmap(datagrid, marker=".", ax=ax)
    ax.set_title("Time {0:.2f}, R = {1:.2f}".format(tspan[i], abs(order(X[i,
plt.show()

```



In Question 1 the convergence happens in "patches" and we need a stronger interaction coefficient K to appreciate the synchronization on the time scale used in the simulation. For the all-to-all interaction matrix the synchronization is "fast" even for a weak interaction coefficient ($K = 0.001$), and happens "uniformly".

Question 3:

Generate a random adjacency matrix where $\mathbf{A}_{ij} = 1$ with a probability p , where a 'success' will generate $\mathbf{A} = \mathbf{1}$ and $\mathbf{A} = \mathbf{0}$ otherwise. Which probability is needed (approximately, based on the final state) in order to retain synchronized oscillations given your chosen σ ?

Use again the function *heatmap*. You should plot only the final state for the different p (both bigger and smaller than the critical probability).

```

In [12]: start = time()

fig, axs = plt.subplots(4, 5, figsize=(20, 16))
axs = axs.flatten()

P = np.linspace(0, 1, 20)
R = np.zeros(shape=(len(P),))
M = 5

for k, p in enumerate(P):
    A = A_alltoall(N, p)

    K = 0.001

    # simulate neurons
    X = odeint(model, l_x0, tspan, args=(l_f, K, A))
    X = np.reshape(X, (X.shape[0], int(N**0.5), int(N**0.5)))
    datagrid = np.sin(X[-1, :])
    heatmap(datagrid, marker=".", ax=axs[k])

    r = 0
    for l in np.arange(M):
        r += abs(order(X[-(l + 1), :]))
    R[k] = r / M

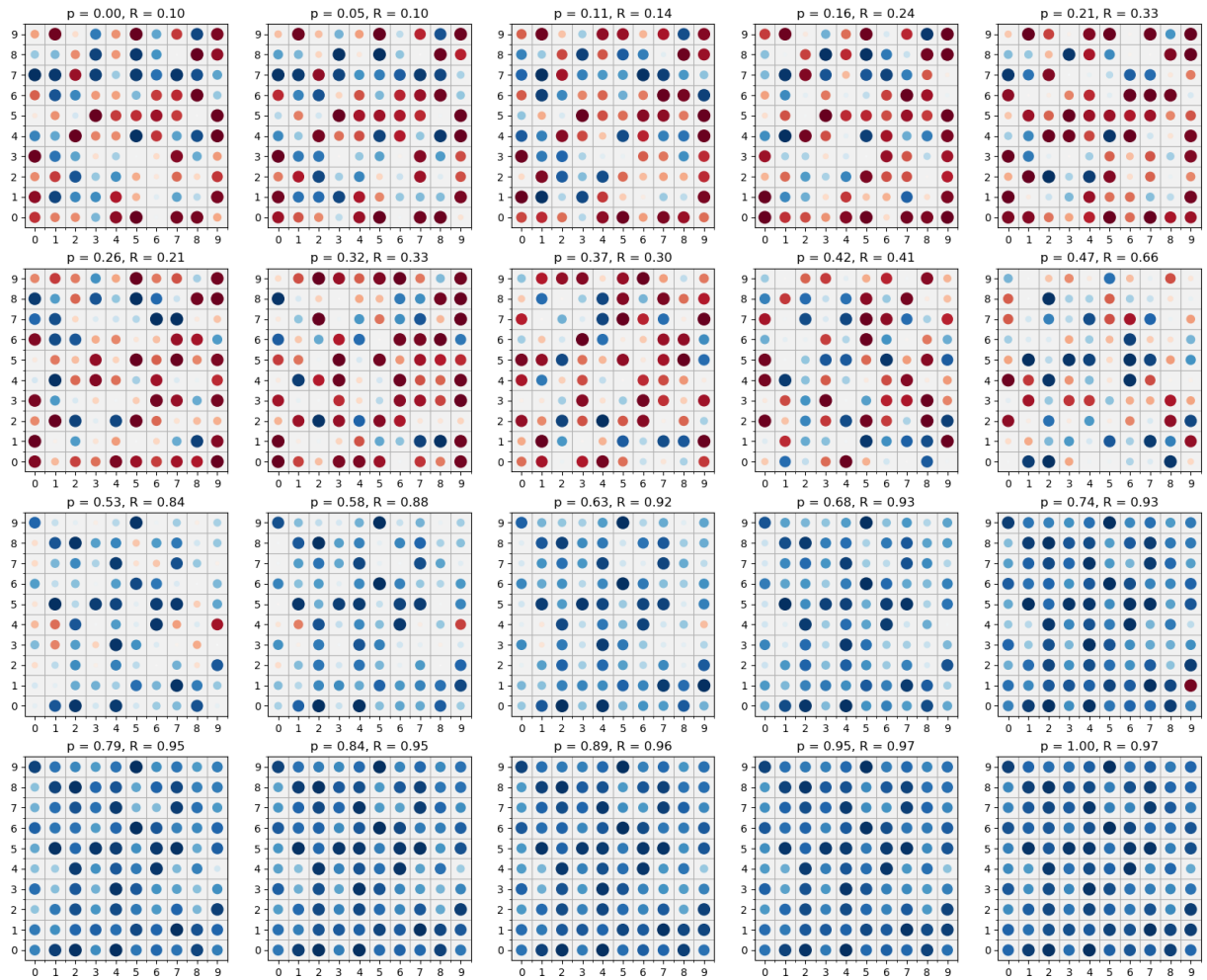
    axs[k].set_title("p = {0:.2f}, R = {1:.2f}".format(p, R[k]))

end = time()

print("It took ", end - start, " s.")

```

It took 57.32160305976868 s.



Question 4:

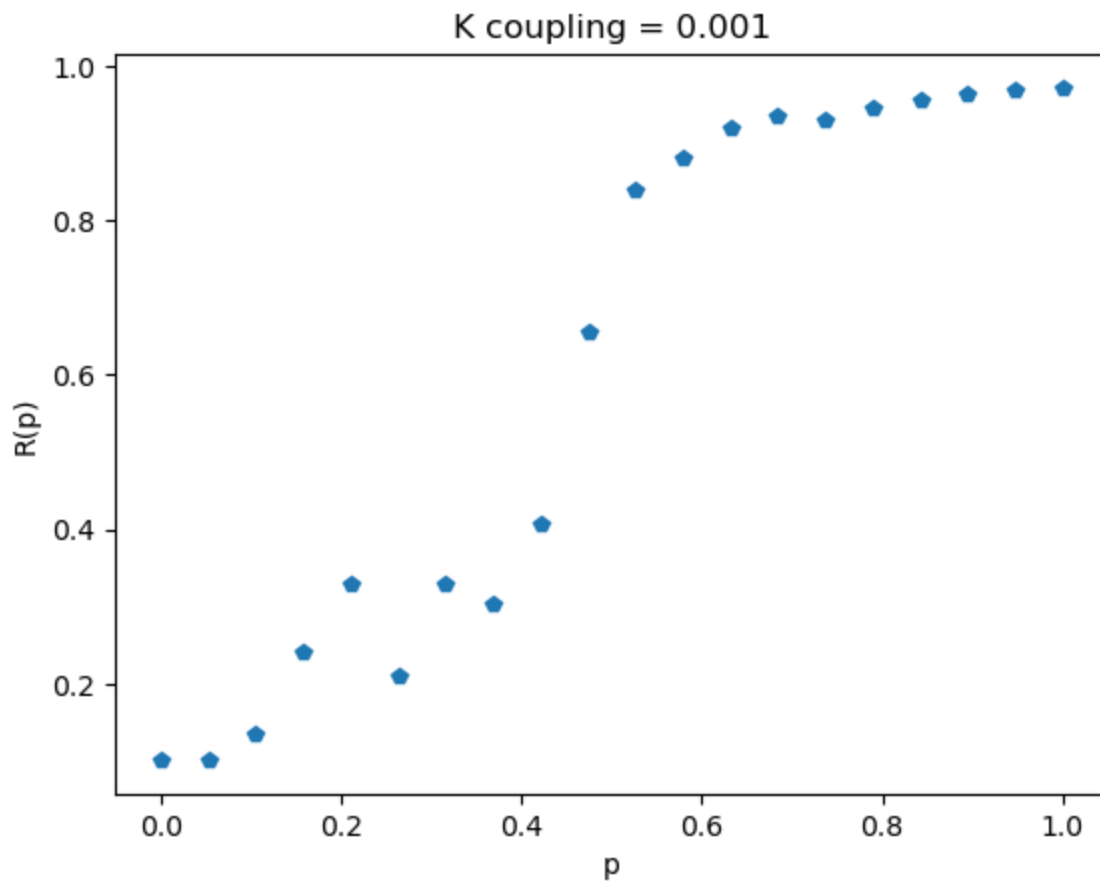
With R defined as $R = \frac{1}{N} \sum_j e^{i\theta_j}$, plot the function $R(p)$ and find the critical probability (the probability of the neuron connections when the system becomes synchronized $\sim R \geq 0.5$). Use at least 10 different values of p for the plot.

Hint: to have a "reliable" estimate of R , you could average it on some time (at the end of the simulation).

Which is the critical value of p ?

```
In [13]: plt.plot(P, R, "p")
plt.title('K coupling = ' + str(K))
plt.xlabel("p")
plt.ylabel("R(p)")
```

```
Out[13]: Text(0, 0.5, 'R(p)')
```



$R \geq 0.5$ is attained for $p \sim 0.5$.

B. The Kuramoto branches (Optional)

```
In [14]: # import important libraries
from scipy.integrate import odeint, quad
# from IPython.display import set_matplotlib_formats
from matplotlib.markers import MarkerStyle
# set_matplotlib_formats("png", "pdf")
```

Take the self consistent equation:

$$r = \langle \cos(\theta) \rangle_s = rK \int_{-\pi/2}^{\pi/2} \cos^2(\theta) g(Kr \sin(\theta)) d\theta$$

And use it to plot the 2 branches stemming from the Kuramoto's model in the plane (K,r)

hint:

the curve is the made by the set of points in plane (K,r) such that:

$$0 = rK \int_{-\pi/2}^{\pi/2} \cos^2(\theta) g(Kr \sin(\theta)) d\theta - r = K \int_{-\pi/2}^{\pi/2} \cos^2(\theta) g(Kr \sin(\theta)) d\theta - 1$$

Define function that finds $F(K, r) = K \int_{-\pi/2}^{\pi/2} \cos^2(\theta) g(Kr \sin(\theta)) d\theta - 1$

than find F(K, r) for a mesh grid of points, and finally select the curve such that F(K,r)=0

```
In [15]: si_w = 1
Kc = 2 / np.pi * np.sqrt(2 * np.pi) * si_w

'''
The self/consistent equation (6.14) gets rewritten such that
'''
def integrand(x, K, r, sigma):

    return (
        np.cos(x) ** 2
        * np.exp(-((np.sin(x) * K * r) ** 2) / (2 * sigma**2))
        / (np.sqrt(2 * np.pi) * sigma)
    )

def integral(K, r, sigma):
    return quad(integrand, -np.pi / 2, np.pi / 2, args=(K, r, sigma))

def F(K, r):
    return K * integral(K, r, si_w)[0] - 1
```

```
In [16]: # once defined the function F(K,r) we can plot it
# we use the contour function to have the F=0 slice
```

```
contr = np.arange(0, 1.1, 0.01)
contK = np.arange(0, 5, 0.1)
KK, rr = np.meshgrid(contK, contr)
V = np.array([0.0])
Z = np.zeros_like(KK)

for i in range(KK.shape[0]):
    for j in range(KK.shape[1]):
        Z[i, j] = F(KK[i, j], rr[i, j])
plt.contour(KK, rr, Z, V, colors="purple")
plt.plot([0, 5], [0, 0], color="purple")
plt.scatter(Kc, 0)
plt.xlabel("K")
plt.ylabel("r")
plt.show()
```

