FUNDAMENTALS OF MATLAB

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1. Introduction to MATLAB

1.1. MATLAB windows, variables and output.

MATLAB (Matrix Laboratory) is a language for technical computing. It is based on matrix (array) operations; It integrates computation, visualisation, and programming and is a numerical software.

1.1.1. MATLAB Tabs. There are various tabs that can be used to carry out tasks, interactively (see figure 1). These include the Home tab (where you can create new scripts, open previous ones, set preferences, etc) and the Apps tab (add ons to MATLAB to enable other functionalities, e.g. curve fitting, image processing, statistical analysis, optimisation, etc). Other tabs have functionalities relevant to other tasks.

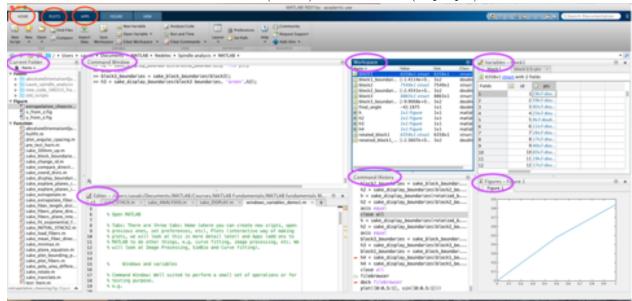


FIGURE 1. Tabs (in red) and Windows (in purple).

1.1.2. MATLAB Windows. (See figure 1)

Command Window: The command window is suited to perform a small set of operations or for testing purposes. e.g. type the following in the command window and see what happens:

```
2 + 2
or
% display i = from 1 to 10
for i = 1:10
i
end
```

Note: The symbol % indicates to MATLAB that it can ignore whatever is on the same line and follows the %, so you can use this to make comments on commands, to clarify to others (and remind yourself) of what you are intending to do.

Variables: Variables are characters that represent a value. To initialize a variable with a value, the operation = is used. e.g.

```
my_variable = 2 + 2
```

This variable will have the value of 4. So whenever you type my_variable on the command window, it will output the value 4.

Variable names must start with a letter and can contain numbers and other symbols. Almost any word can be assigned to a value, with a few exceptions. To check which words cannot be used as variable names, type iskeyword in the Command Window:

iskeyword % none of these words can be used to name variables.

Suppress output on the Command Window: MATLAB prints out the result of whatever operations you perform on the Command Window. If you want to avoid this, use a semicolon at the end of the line.

```
my_vec = [1 2 3 4 5 6 7 8 9 10];
my_sum = sum(my_vec);
```

Workspace Window: This window shows the variables you have defined, their values and information about them. (In case you cannot see the window, type workspace on the Command Window.)

Command History Window: This window display a log of statements that you have ran on the current and previous MATLAB sessions. (In case you cannot see the window, type commandhistory on the Command Window.)

Editor Window: To automatically analyse data or images, or simulate models, it is recommended to write *script* or *function files*. The Editor Window facilitates this, by providing a means of collecting all necessary commands for a specific task on to one file. We will learn more about this below. (In case you cannot see the window, type edit filename on the Command Window, where the filename is the name of the file you want to creadte/edit. It will be saved on the current folder, shown on the Current Folder Window (see below).)

Current Folder Window: This window lets you navigate folders. It shows the current working folder, from where you can load variables and files and on which any changes are saved. (To open this window, type filebrowser on the Command Window.)

Variables Window: Displays the values of the variables that are on the Workspace.

Figures Window: Displays figures. It opens when you plot a figure.

1.1.3. Saving your work.

Save the Command Window: It might be helpful to save the commands you use on the Command Window and the output (remember that the Command History records only the commands). To do so, create a .txt file by typing the following on the Command Window:

diary thursday_20th % today is the name of the .txt file where the commands and output after this line will be saved.

```
% Type some commands ...
diary off % stops recording
```

As a measure of safety, make sure that you save your work every now and then, by typing diary off diary on. Commands carry on being saved at the bottom of the text file.

Save the Workspace (the variables you are working with): You might want to reuse the variables you are currently working with, sometime in the future, so it is a good idea to save them. To do that type the following on the Command Window (where the filename is chosen by you)

```
save filename % this saves the variables to a file with .mat extension load filename % this loads the variables to the Workspace
```

Clear the Command Window: type on the command window

clc

Clear the Workspace: type on the Command Window:

clear

Be careful not to confuse the two!

Now try exercise 2.1.

1.2. Arrays and operations on arrays.

MATLAB was originally written to ease dealing with tools of linear algebra - vectors and matrices (here referred to as *arrays*).

An **array** is a multi dimensional grid of data. Tables in Microsoft Excel can be thought of as arrays with dimensions $r \times c \times p$ corresponding to r rows c columns and p pages. In MATLAB it is similar, but using arrays is facilitated. Figure 2 illustrates arrays of different dimensions.

Arrays are fundamental to MATLAB, as all data is stored in this format. It can also be useful to have data in this format; for example, it can make sense to store images as arrays (figure 3) and as we will see, they are ideal to store stoichiometric information of a set of chemical reactions (figure 4).

FIGURE 2. Arrays with different dimensions.

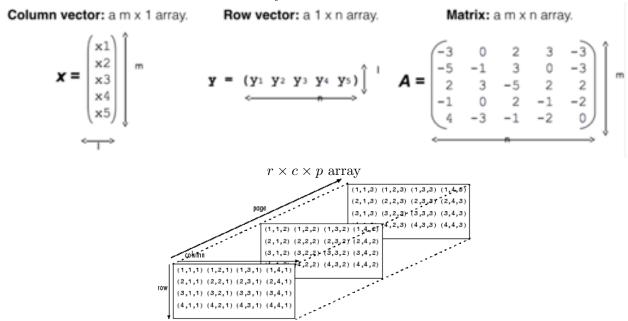
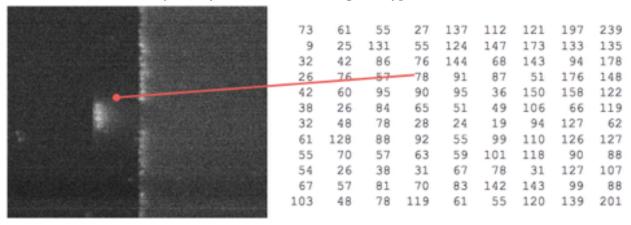


FIGURE 3. An image is a set of data that is real-valued, ordered and represents color and intensity. Arrays are ideal for storing this type of information.



Create arrays: by specifying values using squared brackets, commas, spaces and semicolons e.g.

```
a = [1 2 3 4 5 6 7 8 9] % a row vector, also called a 1x9 array
b = [5; 6; 3; -1; 6; 9; 2; 5; 5] % a column vector, also called a 9x1 array
A = [1 2 3 4 -1 -2 -3 -4; 5 6 7 8 -5 -6 -7 -8] % a 2x8 matrix or array

% Equally spaced arrays
c1 = 1:10 % with a step of 1
c2 = 1:2:10 % increasing with a step of 2
c3 = 10:-2:1 % decreasing with a step of 2
```

FIGURE 4. Stoichiometric information of a simple enzymatic reaction stored in an array.

In-built array functions: MATLAB has in-built tools (called functions) for creating arrays. Note the use - call the function name, provide input to the functions inside round brackets and possibly allocate the result to a new variable.

```
d = linspace(1,20,7) % linearly spaced row vector, between 1 and 20, with 7 entries B = ones(3,3) % a 3x3 array with all entries 1 C = zeros(5,2) % a 5x2 array with all entries 0 D = eye(4,4) % 4x4 identity matrix, i.e. with 0's everywhere, except on the diagonal, which are 1's E = rand(1,10) % 1x10 array with entries in [0,1] randomly chosen E = rand(2,10,10) % 10x10 array with entries either 1 or 2, randomly chosen
```

Indexing: Access and change individual entries in arrays, by indicating the name of the array and the rows and columns inside round brackets. Note the use of ':' to create a range:

```
% acess specific entries of arrays
A(1,2) % is the element of A in col 1 row 2
A(1,1:3) % are the elements of A in row 1, cols 1 through 3
A(1,:) % is all the entries in row 1
A(1,2:end-1) % all the entries in row 1 except the first and last, defined using % the |end| keyword

% Assign values to specific entries in array:
A(1, 2:end-1) = 10 % all entries of row 1 in A, except the first and last, % are equal to 10

% Delete one or more rows of an array:
A(1:2, :) = [] % assign rows 1 and 2 of A to the empty array
```

Linear indexing: all arrays can also be thought of as a one column array, from top to bottom, left to right, so

```
A(2) % accesses element 2 top to bottom, left to right
```

A(:) % displays A as a column vector.

Logical indexing: You can use the logical operators >, >=, <, <=, ==, |, & (greater than, greater than or equal to, less than, less than or equal to, equal, or, and) to test entries in arrays, as follows:

Arithmetic with Arrays: Addition, multiplication, substraction, division, powers.

```
a*b % standard array multiplication (see figure 5A)
a.*b % multiplication element by element (see figure 5b)
a.^2 % raise each element of a to the power of 2
a./2 % divide each element of a by 2
```

% and An, respectively

FIGURE 5. (A). Standard array multiplication. (B). Element-by-element array multiplication.

Array manipulation: Array can be manupulated in many ways. Below are two examples. Other functions include fliplr, flipud, repmat, reshape, sort.

 $large_A = [A, A, A]$; % Concatenates array A on the row direction - i.e. places them next to each other.

B = A' % the transpose of A, it exchanges the rows and the columns

1.3. Help and Documentation.

You have already used many of the tools (functions) MATLAB has on offer. You might want to read more about how those functions are used, and you should! To do so, you can type in the Command Window:

help functionname

You can also check the f_x symbol on the Command Window or google the MATLAB documentation and search the name of the function there.

Now try exercise 2.2.

1.4. Data types.

By now, you already understand what variables are, how to create them (section 1.1) and where and how you can look up information about them (Workspace Window). Now we will learn to understand that information:

Data may come in many different forms, for example, numerical (e.g. intensity values of a FRET imaging experiment), textual (e.g. names of proteins) or more complex (e.g. both of the above). In theory, you could have all your data as an array, but in practice, it may make more sense to make use some of the other variable types that MATLAB has, such as *cells* and *structures* (amongst others). The *class* or *type* of the variable describes the characteristics of the variable and the manipulations that can be applied to it.

Numerical variables (default data type): Arrays that have integer and floating point data e.g.

```
a = 1.5;
A = randi(10,10);
```

Logical or boolean variables: Arrays that have true or false data, displayed by 1 or 0 respectively. They are created by relational operators, as seen above (see also in Documentation, Logical Operators, for more details). e.g.

```
B = a > 1;
C = isempty(A);
```

Textual/string variables: arrays with strings and characters, specified using ' ':

```
A = 'John'
```

Structure variables: A structure array is a data class that groups related data using containers called **fields**. Each field can contain any type of data. Let's create a *structure variable*, called **fiber**, which we will use to store locational information on dummy microtubules that make up a mitotic

spindle: fiber has two fields called id and pts which contain information about the fiber id and the (x, y, z)-coordinates of the points that make up a fiber, respectively.

When you open the variable fiber in the Variables Window, it should look as in figure 6.

To access data in a structure variable, use the row number and the field name: structName(i).fieldName. For example, if you want the coordinates of fiber 2, type fiber2_pts = fiber(2).pts.

Cell Variables: Arrays that can contain data of varying types and sizes - compare with standard arrays and structure arrays. To define:

```
myCell = {1, 2, 3; 'text', rand(5,10,2), {11; 22; 33}}
% This cell variable has 6 entries: the first three are of numerical type,
the 4th is of character type, the 5th is again numerical and the 6th is a cell
(a cell inside a cell).

myCell2 = cell(2,3) % this is an empty cell with 2 rows and 3 columns
```

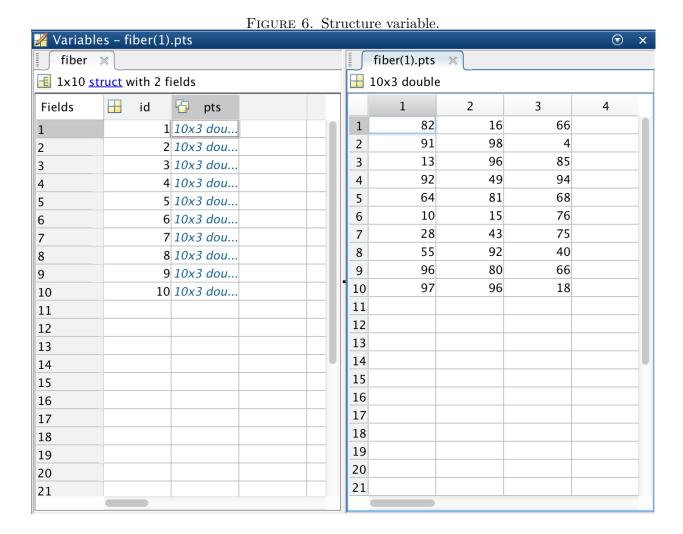
You can see the class/type of your variables on the Workspace Window or by typing whos on the Command Window. For further information on these and other variables, see the MATLAB documentation.

Now try exercise 2.3.

1.5. MATLAB Functions (tools) to manipulate arrays.

To manipulate arrays, you have already used MATLAB functions such as find, size and cat. Here are some of the general rules when it comes to using these, along with some examples. Remember that you can look these functions up on the MATLAB Documentation.

To use functions, enclose inputs to functions in round brackets:



max(A)

Separate multiple inputs with commas:

max(A,B)

Store output from a function by assigning it to a variable:

$\max A = \max(A)$

Enclose multiple outputs in square brackets:

$$[\max A, location] = \max(A)$$

Basic in-built array functions include:

```
*, /, +, -, /*, ./, .^, log, sin, sum, mean, var, std, max, min, find...
```

To stop execution: ctrl+C

Now try exercise 2.4.

1.6. M-files - scripts.

Instead of running commands on the Command Window one by one, you can collect all of them into one file. This is done on the Editor Window. To open the window, type

edit filename

and replace filename with the name you want to give the file. This will create a new file in your current folder, with extension .m

Let's calculate and plot the sine wave. Type the commands below into a new file on the Editor Window, save the file and run it by simply calling the name of the file on the Command Window.

Now try exercise 2.5.

2. Introduction to MATLAB - Exercises

2.1. MATLAB Windows, variables and output.

- (1) If you haven't done so already, start a MATLAB session.
- (2) Create a diary to save the Command Window.
- (3) Using the command window:
 - (a) Compute the following quantities and assign them to variables.
 - (b) Suppress the output of some of them.
 - (i) 1111-345
 - (ii) $\cos(0.1)$
 - (iii) $\log(\cos(0.1))$
- (4) Save your Workspace and finish saving the Command Window to your diary.
- (5) Clear the Command Window but not the Workspace.

2.2. Arrays and operations on arrays.

- (1) Create a 3×3 random integer array A and two 3×1 integer vectors **a** and **b**. (Hint: type help randi in the Command Window).
- (2) Multiply a by the scalar 5 and name this new vector c.
- (3) Compute a'*b, a*b' and the element-wise product of a and b. What do you get? Why? (Hint: help transpose is helpful here).
- (4) What do you get for A(1,2), A(:, 3), A(1:2, 1:2)?
- (5) Replace the second column of A with b (Hint: the indexing section above is helpful).
- (6) Extract the following from A:
 - (a) row 2, column 1
 - (b) row 3, all columns
 - (c) rows 2,3 columns 2,3
- (7) Compute the (standard array) product of A and b. What do you get? Can you do the element-wise product? Why/why not?
- (8) Concatenate b with itself 3 times to get a 3×3 array B.
- (9) Multiply A and B element-wise and assign the result to a new variable C.
- (10) Use the MATLAB function size to save the dimensions of C in rC and cC. If necessary, use the MATLAB help by typing help size in the Command Window.
- (11) Use help to get information about length how does it differ from size?
- (12) Delete the first row of C.
- (13) What are the dimensions of this new array?
- (14) Find the elements of C that are less than 5, both in linear indexing and row and column indexing.

2.3. Data types.

- (1) Create a string (or char) variable name with your name.
- (2) Create a string (or char) variable sentence with a statement that make sense when you put it together with the string variable name.
- (3) Concatenate the variables name and sentence into new_sentence. Remember that you can use squared brackets of the function cat.
- (4) Generate a random integer matrix K and a zeros matrix L, both of the same dimensions. Create a logical variable M to the relational operation K == L.
- (5) Create a structure called molecules with three fields: name, weight and test, and two entries for each field (make up the data).
- (6) Use the Workspace and the commands who and whos to get information about the variables that you currently have and make sure you understand it.

(7) Use the Variables Window to examine the variables you have created. To do this, simply double click on the variable you want to inspect.

2.4. MATLAB Functions to manipulate arrays.

- (1) Create a 24 × 3 matrix Q. You can think of Q as representing some biological data.
- (2) Calculate minimum, maximum, mean and standard deviation of each column of Q. Use help for find out about the functions min, max, mean and std.
- (3) Get the row numbers where the maximum data values occur in each data column. Remember to specify output parameters to return these.
- (4) Substract the mean from each column of the matrix. (Hint: the repmat function is helpful here).
- (5) Save your current Workspace.

2.5. Script files.

- (1) Write a script file that creates a random vector with 1,000 elements, computes the sum of the squared elements of this vector (see help sum) and outputs the resulting sum.
- (2) Use tic toc to see how long it takes the computer to do this takes (see help tic)

3. Introduction to programming

3.1. M-files - functions.

You can write your own functions, which would work similar to the MATLAB functions that you have used above (e.g. size, length, etc). That is, your functions should take input values, which are variables saved on the Workspace, and they will give you output, which ideally, you would assign to other variables. Like scripts, functions are also written on the Editor Window, and they also have a .m extension. But they differ from script files. (We will discuss the differences later.)

The example below shows the structure of a function file (type these commands onto a new file on the editor window and save as my_factorial.m):

```
function f = my_factorial(n)
%
% f = my_factorial(n) is a function that calculates the factorial of
% any integer. It takes in one input, which must be positive integer
% value and outputs the factorial of that input, i.e. $(n*(n-1)*...*1)$.
%
f = prod(1:n);
```

Line 1 indicates to MATLAB that this is a function file, that it has an output (f), the name of the function (my_factorial) and that it requires an input (n). Lines 2-6 are comments that explain what the function does and how to use it. Line 7 is blank and line 8 has the commands that define the output, given the input. In summary, the parts of function are the definition of the script as a function, a name, formal parameters (input/output (return)), specification and body.

Once you have saved the function to an .m file, type in the Command Window

```
help my_factorial
```

The comments that explain the function show up, just like for any other MATLAB function. Now try using this function like any other MATLAB function, e.g. as follows:

```
f10 = my_factorial(10)
```

This should output f10 = 3628800.

Function files can have as many inputs and outputs as you like. Here is how:

If your function accepts more than one input:

```
function V = cell_volume(x, y, z)
```

If more than one output is needed:

```
function [pull drag] = motor_movement(x)
```

If no output is needed:
function my_fun(x)
 or
function [] = my_fun(x)

Note of precaution: Remember that you need to make sure that your function works on arrays with dimensions that make sense for what you intend to do. So do not forget taking care of .*, sizes, etc. Note that my_factorial currently only works on arrays with dimensions 1x1.

Note: Remember to make comments and add a help section to all your functions! This looks like unnecessary work, but when you start writing very long programs, it will save you a lot of time.

Now try exercise 4.1.

3.2. Scripts vs functions.

See table 1.

Table 1.

	Scripts	Functions
	Contain MATLAB code.	Contain MATLAB code.
	Stored in files with a .m extension.	Stored in files with a .m extension.
\neq	Scripts execute a series of MATLAB state-	Functions accept input arguments defined
	ments; 'input' must be defined in script or	in the workspace only, execute a series of
	the Workspace; outputs all variables cal-	MATLAB statements and produce only
	culated.	specific output.
#	Not easily used for modulation of your	Easily used for modulation of your pro-
	programs.	grams.

For example:

write a *script* called triangle_area with the commands below and run it by calling the name of the file on the Command Line

```
b = 5;
h = 3;
a = 0.5*(b.* h)

vs

make a *function*

function a = triangle_area(b,h)
%
```

```
% Description:
% Calculates the area of a triangle
%
% Input:
% |b| is the base
% |h| is the heigh
%
% Output:
% |a| the are of the triangle
%
% Area of triangle
a = 0.5*(b.* h);
```

Now call in the Command Window as follows

```
a1 = triangle_area(1,5)
a2 = triangle_area(2,10)
a3 = triangle_area(3,6)
```

Now try exercise 4.2.

3.3. Flow control and loop constructs.

Up to now, you have mostly run commands basically in a straight line - your scripts ran starting at the top and went to the bottom where they ended. If you made a function you could run that function later.

To really create a 'program', you need line programs, branching and iterations. These tell the computer how to make decisions, rather than just run from top to bottom and to run certain commands more than once. These are achieved by using *programming constructs*, such as *if statements*, for loops, while loops (amongst others).

3.3.1. if statement.

See if you can figure out what the program below does:

```
w = randn % a random number between 0 and 1
v = rand(3,3); % a 3x3 array with entries random values

if v < w
    disp('There is at least one element in v that is less than w')
else
    disp('All elements of v are greater than w')
end</pre>
```

Notice that to build if statements you use Boolean expressions with the logical operators that you encountered earlier, such as <, <=, ==,

This program branches in the sense that commands are not ran from top to bottom, but rather only when a specific condition is satisfied (True) then the commands that follow are ran.

3.3.2. for loop.

See if you can figure out what the program below does:

```
for i in [1,2,3,4,5,6,7,8,9,10] % start at i = first entry of [1,2,3,4,5,6,7,8,9,10] % loop i through the vector and equate it to that value disp('This is count ') i % display i on the Command Window end % go to the next value or, if finished, exit the loop
```

So a for loop executes the statements inside the loop a determined number of times (in this case, 10).

3.3.3. while loop.

A while loop tests a boolean statement to be True, like the if statement, and executes the code block under it as long as a boolean expression is True. For example:

Summary note on programming: Algorithms or programs are a set of instructions, a flow control and a termination condition that enable you to automate calculations. Functions provide structure/decomposition of programs into self-contained units of functionality that can be reused, and also abstraction, in order to (re)use them as sort of black boxes.

Now try exercise 4.3.

3.4. Brief on debugging.

It is very unlikely that as soon as you write a program, it works perfectly. Most of the time, you will need to debug it. The process of debugging is facilitated if you know the kind of errors that can come up.

What defines a programming language?

- Syntax: tells us which sequences of characters and symbols constitute a well formed (not necessarily meaningful) string, e.g. x = 3+3 is a string, but x = 3 3 is not.
- Static semantics: tells us what well-formed strings have meaning, e.g. 3/abc is not allowed.
- Algorithms: the collections of commands with correct syntax and static semantics that carry out a specific calculation.

What happens when it goes wrong? (Most common errors color coded with the above categories)

• Typographic errors.

- Wrong use of functions, arrays dimensions do not match.
- Infinite loop
- Unexpected output

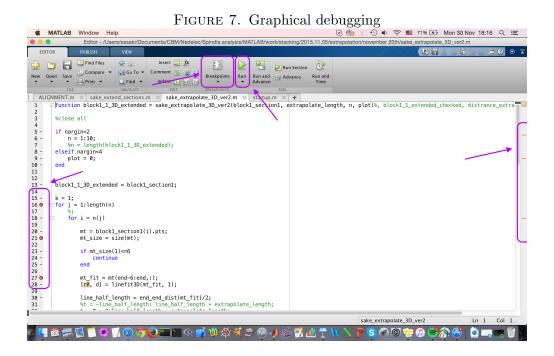
So, to avoid simple errors, the first step is to make sure that you understand the syntax and static semantics of the programming language. The next step is to have a clear plan of what you intent to do in order to avoid algorithmic errors.

MATLAB gives you a lot of help in debugging by characterising the types of errors and providing helpful commands and GUIs.

- 3.4.1. Procedure for debugging from the GUI (see figure 7).
 - (1) Open your program i.e., at the Command Window typeedit your_program.m.

(Do the rest on the Editor Window)

- (2) Check the suggestions on the right hand side and edit as appropriate. Note that not all suggested changes are necessary. Red means deadly error, i.e. the program will not run, orange means that there is a possible error, but the program will run, green means everything is ok.
- (3) Set breakpoints (left hand side) and run.
- (4) Use the step buttons on the panel at the top to step to the next lines.
- (5) Evaluate by looking at the variables' values in the Workspace.
- (6) Continue the run (f5 key).
- (7) Fix the bugs.
- (8) Run again.



3.4.2. Debugging at the command prompt. Many of the techniques discussed in Editor/Debugger have their counterparts at the command prompt. In fact, programatically, you can do further things:

See the help on dbstop for more info.

Now try exercise 4.4.

4. Introduction to programming - Exercises

4.1. Functions.

- (1) Write a function that adds up all the elements of any vector (Hint 1: sum is helpful. Hint 2: this function should have one input and one output.)
- (2) Write a function that takes in any matrix W and returns the largest elements of each column and their position. (Hint 1: sort is helpful. Hint 2: this function should have one input and two output.)

4.2. Scripts vs functions.

- (1) Write a script to get the area, circumference and diameter of any circle, by specifying only the radius.
- (2) Write a function to get the area, circumference and diameter of any circle, by specifying only the radius.
- (3) In the MATLAB documentation, learn about 'program termination' by reading about the command return.

4.3. Flow control and loop constructs.

(1) In each of the following questions, evaluate the value of the variables indicated and then use MATLAB to check your answers.

```
(i)
    if n > 1
        m = n+1
    else
        m = n - 1
    end
    a. n = 7 m = ?
    b. n = 0 m = ?
    c. n = -10 m = ?
(ii)
    if 0 < x < 10
        y = 4*x
    elseif 10 < x < 40
        y = 10*x
    else</li>
```

```
y = 500
end
a. x = -1 y = ?
b. x = 5 y = ?
c. x = 30 y = ?
d. x = 100 y = ?
```

(2) Write a scripts to evaluate the following function:

```
h(T) = T - 10 when 0 < T < 100
= 0.45 T + 900 when T > 100

Test cases:
a. T = 5, h = -5
b. T = 110, h = 949.5
```

- (3) Create an M-by-N array of random numbers (use rand). Move through the array, element by element, and set any value that is less than 0.2 to 0 and any value that is greater than (or equal to) 0.2 to 1.
- (4) In the <u>MATLAB documentation</u>, learn about 'loop control' by reading about the commands break and continue.
- 4.4. **Debugging.** Enter the MATLAB program below to a script in the MATLAB editor.

```
% thirty random integers between -10 and 100
v = round(-10.0 + 110*rand(1,30));

% sum all positive elements of array v
for k = 1:1:length(v)
    if (v >= 0)
result = result + v
    end
end

disp('The sum of the positive elements in v is: ')
disp(result);
```

- Run the program and correct any syntax errors.
- Using the MATLAB Editor, set breakpoint at the lines with the statements:

```
for k = 1:1:length(v)
result = result + v
```

- Debug the program by stepping through the program and watching the Workspace and Command Window for incorrect behaviour. Correct any logic errors. Reset the breakpoints if necessary and rerun the corrected script watching the workspace and command window.
- Correct any style errors.

5. Data import and visual analysis

We will use two biological examples to learn to import and plot data into MATLAB.

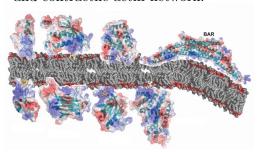
Example 1 - Contractile actin network. In animal oocytes, the nucleous is much larger than in somatic cells. As a result, during meiosis I, chromosomes have to travel long distances to get to the spindle. Microtubules (MT) are involved in the recruiting of the chromosomes, but due to rapid turnover of the filaments their maximal length is limited, and chromosome capture is inefficient at distances greater than $40\mu m$ away from the centrosomes. See figure 8.

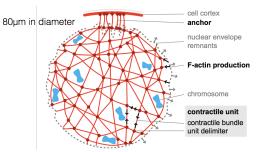
It is known that an F-actin contractile network transports chromosomes to within capture range of MT asters. However, the exactly ingredients that make up this network are currently unknown.

The data in the .txt file is the result of a simulation of a contractile network that contains actin filaments, cross linkers and molecular motors. Specifically, the data corresponds to the positions of the filaments (in x, y), at every second, for 10 seconds. Note that in this simulation, the centre of the nucleus is (0,0), there are 500 fibers and the network contracts towards the middle rather than the apex.

The goal is to use MATLAB to check whether this network is contacting (and, if you have enough time, at what rate, in order to compare with experimental measurements and draw a conclusion about the current model of the contractile network).

FIGURE 8. Left: Lipids on membranes act as docking sites for proteins, to facilitate their recruiting. Right: Schematic of the nucleus of an animal oocyte, chromosomes and contractile actin network.





Example 2 - Protein recruitment by membrane lipids.

Many cellular processes require the recruitment of proteins to specific membranes. As illustrated in figure 8, membranes are decorated with lipids that act as docking sites for proteins.

To study this membrane functionality, an experiment has been carried out to measure cooperativity between some of the most common (phosphoinositide)-binding target. The excel file contains data on lipid protein interaction, with single lipids and lipids in cooperation. We will use MAT-LAB to visualise this data and draw conclusions on whether cooperation has enhancing or inhibiting effects.

5.1. **Data import.** Data can be imported interactively, using the Import Data button on the Home tab, or programatically, using the commands listed in the <u>documentation</u>.

See exercise 6.1

5.2. Making and editing figures.

The following commands show you how to make figures programatically.

```
% Create graph in new figures
x = linspace(0,2*pi,100);
y = sin(x);
z = cos(x);
               % define new figure
figure (1)
plot(x,y);
figure (2)
              % define new figure
plot(x,z);
% Plot multiple images in the same figure
x = linspace(0, 2*pi, 100);
y = \sin(x);
z = cos(x);
plot(x,y);
hold on
            % stay in current figure
plot(x,z);
hold off
           % finish
% add title, axis labels and legend
title('\sin(x) and \cos(x) for x between 0 and 100')
xlabel('-2\pi < x < 2\pi') % x-axis label
ylabel('sine and cosine values') % y-axis label
legend('sin(x)','cos(x)')
% Change lines colors, width and markers.
x = linspace(0, 2*pi, 100);
y = sin(x);
z = cos(x);
figure (1), plot(x,y, '*')
                                                       % plot data points
figure (2), plot(x,z, '--ro', x, z, 'LineWidth', 2) % plot line
% save figure for future editing (MATLAB file)
savefig('fig1');
% save figure to one of the standard formats
saveas(figure(1), 'sin_cos_fig', 'png');
% Subplots in same figure
x = linspace(-5,5); % define x
                        % define y1
y1 = \sin(x);
y2 = cos(x);
                       % define y2
figure
                       % create new figure
subplot(2,1,1)
                       % first subplot
plot(x,y1)
title('First subplot')
subplot(2,1,2)
                       % second subplot
```

```
plot(x,y2)
title('second subplot')

% Discover how to make cool graphs and figures
%http://uk.mathworks.com/discovery/gallery.html?refresh=true
```

To make figures interactively, select a variable in the Workspace and look on the Plots tab. It shows you the recommended plots for that variable. The Plot Tools can be used to edit the figure aesthetics.

Now try exercise 6.2.

6. Data import and visual analysis - Exercises

6.1. Data import.

- Import the Contractile Actin Meshwork data, as a numerical array, using the Import Tool. Take care to specify the delimiters, the data that you want to import and what variable type to use to store the data in MATLAB.
- Import the Lipid-Protein Interactions data, as a numerical array, programatically. To do so you need to inspect the data to understand how it is organised and what exactly you would like to import, given the question you want to answer. Next, read the documentation on the command xlsread and use it to import the data.

6.2. Making and editing figures.

• Plot the lipid-protein interaction data interactively. You should have already imported the data using

```
xlRange = 'B2:X96';
filename = 'protein_lipid_interaction.xlsx';
lpMAT = xlsread(filename, xlRange);
```

Now that you have imported the data of the lipid-protein interactions, highlight the corresponding variable(s) in the Workspace and explore the Plots Tab to choose the most appropriate plot to use. Remember that the aim is to compare single and double lipid-protein interactions. Edit, annotate and save your figures and draw conclusions. (Hint: Try to plot a heatmap.)

• Plot the Contractile Actin Meshwork data. You should have already imported the data using the Import Tool, as a numeric matrix, and named it 'ActinMAT'.

Plot the data such that on the x-axis you have time and on the y-axis you have the distance from the centre of the nucleus. Remember that fibres are followed for 10 seconds, there are 500 fibres and they contract toward the centre and not the apex. Note that a fiber is made up of many points, but it is enough to follow the trajectory of only one (reference) point of each fiber. Remember that we want to know if the network contracts, an maybe other parameters, such as speed of contraction. Edit, annotate and save your figures and draw conclusions.

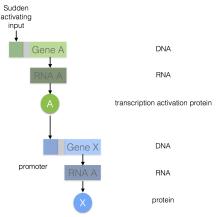
7. More on MATLAB functions

The aim of this section is to have more practise on using MATLAB functions, reading and understanding the documentation and in general writing programs in MALTAB. We use specific examples of using MATLAB to simulate mathematical models of biological systems and to perform segmentation of a collection of images.

7.1. Mathematical modelling of regulatory networks of gene transcription. To meaning-fully assess the biological impact of any interaction in the cell, we need to know how molecules interact (concentrations, affinities, kinetic behaviours) and how behaviours of the molecules change over time, i.e. the dynamics of the species.

We begin with the simple system illustrated in figure 9: A gene encoding the activator gene geneA will produce as its product protein A, via an RNA intermediate. Protein A will then bind to the regulatory promoter of gene geneX, p_X , to form the complex $A:p_X$. Once it is formed, it stimulates the production of an RNA transcript that is subsequently translated to produce protein X.

FIGURE 9. Some of the biochemical steps in the activation of gene expression by a transcription activator.



We are interested in knowing when transcription is induced. Therefore we concentrate on understanding the interaction between protein A and the promoter region p_X . Specifically, we will investigate the amount of bound promoter complex $A: p_X$.

Note that complex $A: p_X$ can dissociate, and this is illustrated with the following notation:

$$(1) A + p_X \rightleftharpoons A : p_X$$

Recall that the formation of the complex $A: p_X$ (between two binding partners A and p_x) depends on the **rate constant** k_{on} , which describes how many productive collisions occur per unit time, per protein, at a given concentration of the substrates. Similarly, there is a dissociation constant k_{off} . The rate of complex $A: p_x$ formation equals the product of the rate constant and the concentrations of the substrates. Similarly, the complex dissociation occurs at a rate k_{off} multiplied by the concentration of the complex. These are called the **rates of the reactions**. So we have:

rate of complex formation =
$$k_{on}[A][p_X]$$

rate of complex dissociation = $k_{off}[A:p_X]$

7.1.1. At steady state.

Let us consider the **steady state** of this system. The steady state is the moment when chemical equilibrium is attained; there is no net change in free energy to drive the reaction in either direction and, as a result, association rate = dissociation rate. Therefore, an **equilibrium constant**¹, K, can be defined to be the ratio of the association and dissociation constants, at equilibrium:

association rate = dissociation rate
$$\Rightarrow k_{on}[A][p_X] = k_{off}[A:p_X] \Rightarrow \frac{[A:p_X]}{[A][p_X]} = \frac{k_{on}}{k_{off}} = K$$

Therefore, the amount of bound promoter complex $[A:p_X]$ at equilibrium is $K[A][p_X]$; that is:

$$[A:p_X] = K[A][p_X]$$

Now, let's consider what happens when the concentration of A increases by, say, a factor of 10. Intuitively from equation (1), we know that $A:p_X$ should increase too, but we can not determine the amount of the increase without additional information (the concentrations of the components and the affinity of the binding interaction. In general, we know the total concentrations of the reactants, and not the concentrations of the bound and unbound species (which are [A] and $[p_X]$). Since in a cell there are typically many copies of A, but only one or two copies of p_X (i.e. one gene of X per haploid genome), as far as A is concerned, it is safe to assume that $[A:p_X]$ is negligible, relative to the total amount of A, A^T . So we preserve the notation A to denote the total amount of A. For p_X , the total concentration of p_X is $[p_X^T] = [p_X] + [A:p_X]$. We can rewrite the amount of bound promoter in terms of the total concentration of p_X :

(2)
$$[A:p_X] = K[A]([p_X^T] - [A:p_X])$$
$$\Rightarrow [A:p_X] = \frac{K[A]}{1 + K[A]}[p_X^T]$$

We are now ready to determine the effect of incrementing the concentration of A on the number of complexes $[A:p_X]$ at steady state: Suppose $K=10^8M^{-1}$, $[A]=10^{-9}M$, $[p_X^T]=10^{-10}M$ (under the assumption that there is one copy of the gene in a haploid cell, e.g. with a volume of $2\times 10^{-14}L$). Then, by $[A:p_X]=\frac{K[A]}{1+K[A]}[p_X^T]$, a 10-fold increase of [A] from $10^{-9}M$ to $10^{-8}M$, increases $[A:p_X]$ 5.5-fold, from 0.09×10^{-10} to 0.5×10^{-10} . In other words, a 10-fold increase in [A] induces a 5.5-fold increase in transcription of X.

To assess the biological impact of a change in transcription activator levels, it is also important to determine the fraction of the target gene promoter that is bound by the activator, since this is directly proportional to the activity of the gene's promoter. So rearrange equation (2):

(3)
$$[A:p_X] = \frac{K[A]}{1+K[A]}[p_X^T]$$
$$\Rightarrow \frac{[A:p_X]}{[p_X^T]} = \frac{K[A]}{1+K[A]}$$

¹The equilibrium constant measures the binding strength between molecules; It is larger the greater the binding strength. Half of the binding sites are occupied by the ligands when the ligand's concentration reaches a value of 1/K.

This shows that when [A] = 1/K, the promoter p_X has a 50% chance of being occupied and when [A] > 1/K the bound fraction is almost equal to 1, so p_X is almost fully occupied and transcription is maximal.

7.1.2. Differential equations help understand transient behaviour. We have looked at the dependancy of regulatory systems on molecular interaction, at steady state. Equation $[A:p_X] = \frac{K[A]}{1+K[A]}[p_X^T]$ tells us that when [A] is changed, $[A:p_X]$ at steady state also changes. **However, this change is not immediate.** The behaviour of a regulatory system, over time provides some of the most important and basic insights. Understanding the behaviour of a system over time is the central theme of 'dynamical systems' and for which the mathematical subject of calculus was invented. The general problem is: given the rates of change of a set of variables that characterise the system at any instant, how can I compute future states?

The most common strategy is to use **ordinary differential equations**, which, when describing biochemical reactions (ODEs), have a simple premise:

the rate of change in the concentration of a molecular species Z, denoted by $\frac{d[Z]}{dt}$, is given by the balance of the rate of its appearance with that of its desappearance.

In the case of the complex $A: p_X$:

rate of change in concentration of $A: p_X =$ rate of complex formation – rate of complex dissociation

(4)
$$\frac{d[A:p_x]}{dt} = k_{on}[A][p_X] - k_{off}[A:p_X]$$

Again, at steady state $\frac{d[A:p_X]}{dt} = 0$, the concentration of $A: p_X$ does not change, so $k_{on}[A][p_X] = k_{off}[A:p_X]$.

Calculation of all values of $[A:p_X]$ at all times (i.e. the solution to ODE (4)) allows the determination of the dynamics of $A:p_X$, including knowing the rate at which it reaches steady state. Ideally, you would get an **exact solution**, but to do so, is hard and you would have to use software such as Mathematica (or a mathematician of physicist). The next best thing to do is to use **numerical integration** to get a numerical approximation to the solution, for specific (discrete) times. To do so, we can use MATLAB functions such as ode45 and others.

Now, have a look at the MATLAB documentation for the function ode45. Try to understand what the inputs and outputs are. Then, follow the instructions below to learn how to use this function to obtain a numerical approximation to the solution of the ODE in equation (4). Make sure that you compare what is being done with the explanation in the documentation. At the end of the simulation, you should get something like figure 10.

```
*In a script file named reg_network.m*

function dApXdt = reg_network(t, ApX)

%

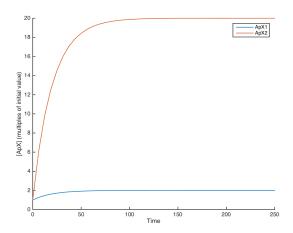
This function defines the odes that describe the transcription

% regulatory network in figure 9.
```

```
% Use with ode45.
% Define parameter values, based on literature
A = 10^{(-9)}; % M
pX = 10^{(-10)}; % M
k_{on} = 0.5*10^7; %sec-1 M-1
k_{off} = 0.5*10^{(-1)}; %sec-1 M-1
% ODE
dApXdt = k_on*A*pX - k_off*ApX;
*in a new script file*
%% solve reg_network for original value of concentration and 10-fold increase
% original concentration
ApXO_init = 0.5e-10;
\% 10-fold increase concentration
ApX0_increase = 0.5e-9;
% time of simulation
tspan = [0 250];
% solve ODE(s) for init. conc.
[Tode, ApXode_init] = ode45(@reg_network, tspan, ApXO_init);
% solve ODE(s) for increased. conc.
[Tode, ApXode_increase] = ode45(@reg_network, tspan, ApX0_increase);
%% visual analysis
% plot original and increase of A in the same figure
figure
hold on
plot (Tode, ApXode_init);
plot (Tode, ApXode_increase);
hold off
legend('ApX_init', 'ApX_increase');
xlabel('Time');
ylabel('[ApX]');
% to facilitate analysis, calculate and plot in multiples of initial value
```

```
ApX_init_num = ApXode_init/ApXode_init(1);
ApX_increase_num = ApXode_increase/ApXode_increase(1);
figure
hold on
plot (Tode, ApX_init_num);
plot (Tode, ApX_increase_num);
hold off
legend('ApX1', 'ApX2');
xlabel('Time');
ylabel('[ApX] (multiples of initial value)');
```

FIGURE 10. Dynamics of the concentration of $A: p_X$. Blue line: for $[A] = 10^{-9}$. Red line: for $[A] = 10^{-8}$.



To understand the behaviour of the system, one of the questions one might want to answer is how long it takes $[A:p_X]$ to get to the steady state. The figure (orange line) looks like the steady state is reached asymptotically. To check it is useful to compare the times that it takes to get to 50, 90, 99 % of the steady state, which are about 16, 47 and 90, respectively.

Understanding transient dynamics of biochemical reactions helps us determine the dependance of the dynamics inside the cell on parameters that are specific to the particular molecules involved. For example, the steady state equation indicates that doubling k_{on} and k_{off} does not affect $[A:p_X]$. The analysis done above and in exercise 1 shows the effect of changing [A] 10-fold, on the dynamics of $[A:p_X]$; i.e. whether there is a new steady state and whether there is a change in the speed that it is attained.

Now try exercise 8.1.

7.2. Image processing.

In this section you will write a program that segments the cells of figure segment_cells.png.

The instructions indicate what you need to do and the MATLAB functions you need to use. Make use of the documentation, and in general, the internet, to understand what each task is asking and how to use the MATLAB functions.

```
%close all
%clear
%clc
% import image into MATLAB
-> use function imread and allocate it to a new vatiable
% im has 3 dimensions, so reduce to 1
-> here you can use the array indexing.
% crop image and assign to a new variable
-> again, user array indexing. Assign no new variable.
% visualise both the original and cropped images
-> create a new figure
-> use imshow
% increase the contrast for better visualisation and visualise in new figure
-> use adapthisteq and assign to new variable
% change image to binary (or balck and white) and visualise
-> use im2bw and graythresh; assign to new variable
% "clean up" and visualise in new figure
-> use imfill, imopen and bwareaopen; remeber to allocate to new different variables
% get cell perimeter and visualise
-> use bwperim; assign to new var
% get perimeter overlay and visualise
-> use imoverlay; assign to new variable
% mark a group of connected pixels inside objects that need to be segmented and visualise
-> use imextendmax; assign to new variable
% clean up and overlay and visualise
-> use imclose, imfill, bwareaopen; assign to new vars
-> use imoverlay; assign to new vars
% complement image (0->1 and 1->0) for watershedding, watershed and visualise
-> use imcomplement, imimposemin, watershed; assign to new variables
```

8. More on MATLAB functions - Exercises

8.1. Example - Mathematical modelling.

Come up with a simple model for the central dogma of biology (below) and simulate it using ode45.

$$DNA \to RNA \to Protein$$

$$\downarrow \qquad \qquad \downarrow$$

$$0 \qquad \qquad 0$$

* DNA is conserved

You need to write the biochemical reactions of each reaction, then write the ODEs that describe how each molecule changes. At this stage you are ready to write a MATLAB program to solve the equations and simulate the system.

8.2. Example - Image processing.

- Write a short script that applies the segmentation done in section 7.2 to more than one image.
- Write a script that counts the number of pixels of each color blue, green and red in image count_color_pixels.png and displays the numbers in a histogram.

9. Next steps

Here is a (non-exaustive) list of topics I consider would be good next steps to your continued learning of MATLAB and programming in general.

9.1. Programming.

- Understand the difference between decimal numbers and floating point numbers.
- Algorithmic analysis: How to define efficiency of an algorithm and why does this matter.
- Performance tuning: Useful Matlab tools for understanding your code: mlint, tic/toc, profile on/off/report.
- Learn about numerical approaches for searching (e.g. exhaustive enumeration, bisection search) and numerical approximations to equations (e.g. Euler method, Newton method).
- Learn how to write recursive programs and why they might be useful. Use examples such as solving the problem of the Tower of Hanoi and calculating the Fibonacci numbers.

9.2. Help from other resources.

• <u>MATLAB Central</u> is a wonderful resource - it is a library of thousands of user-contributed MATLAB files and toolboxes that are open source. From here you can look for functions that do specific tasks, to, for example, get inspiration of how to do things, and from where you can also learn how to program by looking at examples.

If you are already implementing a MATLAB program in a pipeline in your lab, there is a chance that whoever wrote it, may have posted the program on MATLAB Central, so when it stops working, the first thing to do is to check if it has been updated and downloading the newest version.

- Your colleagues ask around! There might be people who can help you.
- For mathematical modelling, the <u>Biomodels Database</u> is a repository for mathematical models of biological systems. Many of them are implemented in MATLAB and you can download the code and run it. You could then use them and modified for your research.

10. Final comments

If you have questions, suggestions and corrections for this tutorial, please do not hesitate in contacting me.

11. Bibliography

- Molecular Biology of the Cell, Edition 6, Garland Science.
- MATLAB documentation
- http://www.facstaff.bucknell.edu/maneval/help211/progexercises.html
- https://www.msi.umn.edu/sites/default/files/MATLAB_Tuning.pdf
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