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Introduction

To provide a comprehensive background for the following chapters that focus on the interaction of human mesenchymal stromal cells (hMSCs) with multiple myeloma (MM) cells, this

Multidimensional Data in Biomedical Research

As modern biosciences advance, researchers increasingly encounter datasets that are influenced by a variety of independent variables, such as time, dosage, and environmental conditions. These variables introduce multidimensional complexity into datasets, challenging traditional analysis methods. For instance, cell adhesion studies, which are crucial for understanding cellular interactions and cancer metastasis, often require analyses across multiple time points and varying adhesion molecule concentrations, demonstrating a time-dependent variability that significantly impacts biological interpretations (Rebl et al., 2010; McKay et al., 1997; Bolado-Carrancio et al., 2020).

Multidimensional data encompass datasets where multiple independent variables (factors), such as experimental conditions or measurement modalities, interact to influence one or more dependent variables (outcomes). These interactions often address multiple hypotheses, making it crucial to design analysis strategies that can reveal the true structure and value of the data (Krzywinski & Savig, 2013).

(put the following examples into discussion? Use one example, rest into discussion?)

A primary example of multidimensional data is multiplex RT-qPCR, where the expression levels of various genes are measured across different samples under varying conditions. Here, the dependent variable is typically the fold change expression values derived from $\Delta\Delta C_t$ calculations (Brankatschk et al., 2012). The independent variables include the genes being measured and the experimental conditions under which the samples are processed.

Microscopy data further illustrate the complexity of multidimensional datasets (Rueden et al., 2017). In this context, the dependent variable might be a quantifiable feature, such as cell count or morphological metrics extracted from image analyses. The independent variables can expand immensely to include factors such as well-plate coordinates in a 96-well plate, Z-positions in confocal microscopy, and time points in time-lapse studies.

Lastly, big-data aggregation tools like Metascape provide a rich source of multidimensional data by integrating various dependent variables, such as gene expression fold changes and associated p-values, with independent variables spanning gene identifiers, gene ontology terms, and ontology classes derived from multiple databases (Y. Zhou et al., 2019). Despite the provision of summarized graphical outputs, the raw data often remain in complex, nested formats within Excel sheets, posing significant challenges for hypothesis-driven research.

This extensive integration of multiple dimensions requires sophisticated visualization and analysis techniques. While basic statistical visualizations suffice for one- or two-dimensional data, more complex data sets necessitate advanced techniques, which allow researchers to vi-

sualize and interact with data in ways that elucidate the underlying patterns and relationships (Dunn et al., 2017). However, the gap between available visualization tools and the needs of clinicians or biologists without extensive bioinformatics training remains wide, emphasizing the need for intuitive, user-friendly tools that bridge this knowledge gap and enhance the accessibility of complex data analyses (Dunn et al., 2017).

Nontransparencies in Biomedical Data Analyses

The advent of advanced technologies in biosciences has ushered in an era of Big Data, characterized by unprecedented volumes and complexities of data (Bubendorf, 2001; Yang et al., 2017; Ekmekci et al., 2016). This rise has been paralleled by significant challenges in data analysis, particularly impacting the reproducibility of scientific research. Studies such as the Baker (2016) survey revealed that more than 70 % of researchers have tried and failed to reproduce another scientist’s experiments, highlighting a reproducibility crisis that questions the reliability of scientific findings (Begley & Ioannidis, 2015; Ioannidis, 2005).

Reproducibility is considered foundational to scientific research, ensuring that findings are reliable and verifiable. Still, its meaning requires precise definition (Goodman et al., 2016). The common understanding of scientific reproduction implies not only that detailed information is provided to enable independent repetition (*transparency*), but also that time and effort is invested into repeating the experiments (*corroboration*). However, since modern biomedical journals are demanding novelty research, and since experiments have become highly specialized and time-intensive, repeating someone else’s work is considered neither interesting¹ nor possible for most publications (Flier, 2022; Peng, 2011). Hence, the meaning of reproducibility is confined to *transparency*, a concept that has been applied to many fields, including clinical trials (Goodman et al., 2016; Committee on Strategies for Responsible Sharing of Clinical Trial Data et al., 2015).

Nevertheless, there is a surprising amount of evidence for nontransparencies in biomedical data analyses: For Microarray-based miRNA profiling, raw data was not reported in more than 40 % of 127 articles, making independent verification impossible (Witwer, 2013). The same study also found that re-analysis of data often times did not support the original conclusions. Furthermore, 44 % of 233 preclinical articles describe statistical tests insufficiently, while few don’t describe them at all (Gosselin, 2021). Another study reviewed 147 papers in the field of optometrics and found that 91 % did not discuss their rationale of correcting p-values for multiple comparisons (e.g. Bonferroni correction) (Armstrong, 2014). However, given that the exact use of multiple comparisons corrections has been under debate for decades, it is reasonable

¹Flier (2022): “There are no scientists with the interest, resources, or incentives to “repeat” or confirm this vast sea of published work, so whether the findings they report are reproducible will simply never be assessed.”

to assume that researchers lack the confidence to report their technique in detail (Perneger, 1998; Moran, 2003; Sullivan & Feinn, 2021). Indeed, 77 % of biomedical researchers state that they have not received formal training in data literacy (including visualization and public deposition of data), although they understand its high relevance (Federer et al., 2016). For clinicians, statistical illiteracy is a well-known problem (Lakhlifi et al., 2023). Correspondingly, it has been communicated that there is a lack of simple and intuitive tools to both capture and embed computational work into publications (Mesirov, 2010). Therefore, nontransparencies in biomedical analyses are not only caused by a habit² of insufficient reporting, but could be exacerbated by the confusions caused by currently available methodologies and the lack of proper training.

Semi-Big Data: Big Enough to Cause Problems

Recent advances in big data analysis have significantly improved the standardization of both raw data availability and processing pipelines. Particularly in RNAseq analysis, automation and the use of sophisticated software have established robust standards that enhance reproducibility across studies. For example, tools such as STAR and HISAT for sequence alignment, and Cufflinks and DESeq for differential expression analysis, rely on scripts that standardize processing steps to produce repeatable and verifiable results (Dobin et al., 2013; Kim et al., 2015; Trapnell et al., 2012; Love et al., 2014). These frameworks not only automate data handling but also ensure that data analysis protocols are followed consistently, reducing human error and variability between different users or laboratories.

However, this level of standardization and automation has not been mirrored in the analysis of semi-big data. Semi-big data, as introduced in this thesis, describes datasets that are on the cusp of manageability: substantial enough to overwhelm manual analysis methods yet not sufficiently large or uniform to justify the heavy computational frameworks developed for big data. Such data are frequently generated in experiments like automated microscopy or multiplex qPCR, where the scale and complexity of the data can vary significantly depending on the experimental design and objectives (Krzywinski & Savig, 2013).

Researchers often revert to basic tools such as *Microsoft Excel* for analyzing these semi-big datasets (Incerti et al., 2019). While Excel provides familiarity and immediate accessibility, it lacks the sophisticated data handling capabilities necessary for efficient and error-free processing of complex (multidimensional) datasets. This reliance on manual methods not only makes the analysis laborious and prone to mistakes but also significantly impedes the reproducibility of research findings. The time and effort required to replicate analyses done manually mean that

²Peng (2011): “[...] *old habits die hard, and many will be unwilling to discard the hours spent learning existing systems.*”

validating findings from semi-big data can be prohibitively challenging for peer reviewers and other researchers in the field.

Given these challenges, there is a critical need for developing new tools and frameworks specifically tailored for semi-big data. These tools should bridge the gap between the simplicity of user-friendly software like Excel and the robust, script-based automation seen in big data frameworks. By providing standardized, repeatable, and easy-to-use methods for handling complex datasets, such tools could significantly enhance the reliability and efficiency of research involving semi-big data, ultimately supporting broader scientific inquiry and verification.

The Shortcomings of Common Biomedical Analysis Tools

Interactive software systems commonly used for exploratory data analysis in biomedical research often lack mechanisms to track and reproduce the researcher’s actions systematically. Even when analysis is performed using scripting languages, the integration of results from multiple packages without a coherent record of the commands and code used undermines reproducibility. This practice can obscure analysis, making it difficult, if not impossible, for other researchers to replicate the results (Peng, 2011; Mesirov, 2010; Localio et al., 2018).

A particularly illustrative example is *GraphPad Prism*, a tool ubiquitously employed across biomedical disciplines for statistical analysis. Despite its widespread use, it does contribute to data analysis nontransparencies due to *Prism*’s closed-source nature and the common journal practice of not requiring detailed methodological transparency in its usage, a practice that is common in biostatistics literature (Gosselin, 2021; Localio et al., 2018). Furthermore, *GraphPad Prism* still requires manual data entry and lacks the robustness and automation necessary for handling multidimensional or semi-big data.

Moreover, *Microsoft Excel*, another staple in data processing in biomedicine, is notoriously inadequate for handling multidimensional data and complex statistical analyses. Its limitations include poor error tracking, absence of change documentation (audit trails), and a propensity for introducing errors that often go unnoticed, such as converting gene names to dates (Ziemann et al., 2016). To compensate for these shortcomings, *Microsoft* has recently integrated a Python interpreter into *Excel*, allowing researchers to automate tasks and analyze data efficiently and correctly (Excel, 2023).

Indeed, many common tools in biomedicine allow for scripting or automation to handle semi-big data more effectively. For example, Fiji/ImageJ, a popular image processing platform, supports extensive macro and scripting capabilities (Rueden et al., 2017). These features enable researchers to automate batch processing of image data, streamlining tasks that would otherwise require laborious manual input. Similarly, PyMOL, a leading tool in protein structural biology,

utilizes Python scripting to automate complex tasks, allowing for detailed molecular modeling and visualization that are reproducible and scalable across datasets (Rigsby & Parker, 2016).

Although automation scripts used in tools like Fiji/ImageJ and PyMOL improve transparency for publishing singular data analysis pipelines, they still face challenges that can impede their reproducibility (Peng, 2011; Sandve et al., 2013). These scripts sometimes require specialized software environments, where setting up dependencies and configurations can be complex enough to discourage replication efforts. Additionally, these scripts do not always provide comprehensive outputs of intermediate steps, which is crucial for verifying and understanding the progression of data analysis (Sandve et al., 2013).

On the other hand, when scripts are designed to be more generalized and distributed—for instance, as a Fiji/ImageJ plugin or a standalone application—they can make substantial contributions to scientific research by enabling other researchers to apply these tools to their own data sets (Narzt et al., 1998; Smith et al., 2018). However, this approach also comes with its own set of challenges (Sandve et al., 2013). Often, these generalized tools often lack comprehensive user-manuals (*documentation*) are not thoroughly tested across different platforms or data sets, which can lead to unexpected errors that can not be fixed by the user. Moreover, even when these tools are available, they frequently suffer from low adoption rates, meaning that few people are familiar with the details of such tools, further decreasing the confidence and reproducibility in the final results.

Given these complexities, there is a pressing need for new analytical tools specifically designed for semi-big data. These tools must strike a balance between the ease of use found in basic software and the robust, analytical capabilities of more sophisticated systems. By providing standardized workflows, comprehensive documentation, and ensuring cross-platform compatibility, these tools can significantly enhance reproducibility. They not only allow researchers to perform analyses more efficiently but also ensure that these analyses are robust, transparent, and easily verifiable by the broader scientific community.

This thesis presents a software environment developed in Python, designed to bridge this gap. It demonstrates that even minimal coding skills can be leveraged to create powerful tools that standardize and accelerate the analysis of semi-big data, ultimately fostering more reproducible and trustworthy scientific research.

Modern Standards of Software Development

A main reason to write software is to define re-usable instructions for task automation (Narzt et al., 1998). The complexity of software code makes it prone to errors, which can prevent its usage by persons other than the author himself. This is a problem for the general scientific

community, as the software is often essential for reproduction (Sandve et al., 2013). Hence, modern journals aim to enforce standards to software development, including software written and used by biological researchers (Smith et al., 2018). Here, we provide a brief overview of the standards utilized by `plotastic` that to ensure its reliability and reproducibility by the scientific community (Peng, 2011).

Modern software development is a long-term commitment of maintaining and improving code after initial release (Boswell & Foucher, 2011). Hence, it is good practice to write the software such that it is scalable, maintainable and usable. Scalability or, to be precise, structural scalability means that the software can easily be expanded with new features without major modifications to its architecture (Bondi, 2000). This is achieved by writing the software in a modular fashion, where each module is responsible for a single function. Maintainability means that the software can easily be fixed from bugs and adapted to new requirements (Kazman et al., 2020). This is achieved by writing the code in a clear and readable manner, and by writing tests that ensure that the code works as expected (Boswell & Foucher, 2011). Usability is hard to define (Brooke, 1996), yet one can consider a software as usable if the commands have intuitive names and if the software’s manual, termed “documentation”, is up-to-date and easy to understand for new users with minimal coding experience. A software package that has not received an update for a long time (approx. one year) could be considered abandoned. Abandoned software is unlikely to be fully functional, since it relies on other software (dependencies) that has changed in functionality or introduce bugs that were not expected by the developers of all dependencies. Together, software that’s scalable, maintainable and usable requires continuous changes to its codebase. There are best practices that standardize the continuous change of the codebase, including version control, continuous integration (often referred to as CI), and software testing.

Version control is a system that records changes to the codebase line by line, allowing the documentation of the history of the codebase, including who made which changes and when. This is required to isolate new and experimental features into newer versions and away from the stable version that’s known to work. The most popular version control system is Git, which is considered the industry standard for software development (Chacon & Straub, 2024). Git can use GitHub.com as a platform to store and host codebases in the form of software repositories. GitHub’s most famous feature is called “pull request”. A pull request is a request from anyone registered on GitHub to include their changes to the codebase (as in “please pull this into your main code”). One could see pull requests as the identifying feature of the open source community, since it exposes the codebase to potentially thousands of independent developers, reaching a workforce that is impossible to achieve with closed source models used by paid software companies.

Continuous integration (CI) is a software development practice in which developers integrate code changes into a shared repository several times a day (Duvall et al., 2007). Each integration triggers the test suite, aiming to detect errors as soon as possible. The test suite includes building the software, setting up an environment for the software to run and then executing the programmed tests, ensuring that the software runs as a whole. Continuous integration is often used together with software branches. Branches are independent copies of the codebase that are meant to be merged back into the original code once the changes are finished. Since branches accumulate multiple changes over time, this can lead to minor incompatibilities between the branches of all developers (integration conflicts), which is something that CI helps to prevent.

Continuous integration especially relies on a thorough software testing suite. Software testing is the practice of writing code that checks if the codebase works as expected (Myers et al., 2011). The main type of software testing is unit testing, which tests the smallest units of the codebase (functions and classes) in isolation (Listing 1).

Listing 1: Example of an arbitrary Python function and its respective unit test function. The first function simply returns the number 5. The second function tests if the first function indeed returns the number 5. The test function is named with the prefix “test_” and is placed in a file that ends with the suffix “_test.py”. The test function is executed by the testing framework pytest. Note that code after “#” is considered a comment and won’t be executed.

```
1 # Define a function called "give_me_five" that returns the number 5
2 def give_me_five():
3     return 5
4 # Define a test function asserting that "give_me_five" returns 5
5 def test_give_me_five():
6     assert give_me_five() == 5
```

The quality of the software testing suite is measured by the code coverage, the precision of the tests, and the number of test-cases that are checked. The code coverage is the percentage of the codebase that is called by the testing functions, which should be as close to 100% as possible, although it does not measure how well the code is tested. The precision of the test is not a measurable quantity, but it represents if the tests truly checks if the code works as expected. The number of test-cases is the number of different scenarios that are checked by the testing functions, for example testing every possible option or combinations of options for functions that have multiple options. The most popular software testing framework for Python is pytest, which is utilized by plotastic (Krekel et al., 2004).

Together, the standards of software development, including version control, continuous integration, and software testing, ensure that the software is scalable, maintainable, and usable. This is especially important for software that is used by the scientific community, as it ensures that the software is working as expected at defined versions years after publishing scientific results.

What makes Python an “Easy” Programming Language?

Here, we provide a general overview of the Python programming language, explaining terms like “*type*”, “*method*”, etc., in order to prepare readers without prior programming experience for the following chapters. We also describe the design principles of Python to lay out the key concepts that differentiate Python compared to other programming languages. A more detailed tutorial on Python that’s specialized for bioscientists is found in Ekmekci et al. 2016

Languages such as Python are considered “*high-level*”, which means that it is designed to be easy to read and write, but also independent of hardware by hiding (“*abstracting*”) underlying details (*The Python Language Reference*, 2024). A key principle of Python is the emphasis on implementing a syntax that is concise and close to human language (Listing 2, Listing 3).

Listing 2: Example of readable Python code. This one-line code returns the words (string) ‘Hello, World!’ when executed. The command is straightforward and easy to understand.

```
1 print('Hello, World!')
2 # Output: Hello, World!
```

Listing 3: Example of less readable code written in the low-level programming language C. This code is doing exactly the same as the Python code in Listing 2, but is harder to understand because more steps are needed, including the import of a library `stdio.h` and the definition of a function called `main`.

```
1 #include <stdio.h>           // Import functions for standard input & output
2 int main() {                 // Define a function called 'main'
3     printf('Hello, World!');
4     return 0;
5 }
6 // Output: Hello, World!
```

Furthermore, Python is an *interpreted* language, which means that the code is executed line by line. This makes coding easier because the programmer can see the results of the code immediately after writing it, and error messages point to the exact line where the error occurred. This is in contrast to *compiled* languages, where the code has to be compiled into machine code before it can be executed. The advantage of compiled languages is that the code runs faster, because the machine code is optimized for the hardware.

Python automates tasks that would otherwise require an advanced understanding of computer hardware, like the need for manual allocation of memory space. This is achieved by using a technique called “*garbage collection*”, which automatically frees memory space that is no longer needed by the program. This is a feature that is not present in low-level programming languages like C or C++, that were designed to maximize control over hardware.

Another hallmark of Python is its *dynamic typing system*. In Python the type is inferred automatically during code execution (Listing 4). This is in contrast to *statically* typed languages like C, where the type of a variable has to be declared explicitly and cannot be changed during code execution (Listing 5) (*The Python Language Reference*, 2024).

Listing 4: Example of dynamic typing in Python. The variable “a” is assigned the value 5, which is of type integer. The variable “a” is then assigned the value “Hello, World!”, which is of type string. Python allows dynamic re-assignment of variables with different types. Note that code after “#” is considered a comment and won’t be executed.

```
1 a = 5 # Type integer
2 a = 5.0 # Type float
3 a = 'Hello, World!' # Type string
4 a = True # Type boolean
5 a = False # Type boolean
6 a = [1, 2, 3] # Type list of integers
7 a = {'name': 'Regina'} # Type dictionary
```

Listing 5: Example of static typing in C. The variable “a” is declared as an integer (int), and can only store integers. The variable “a” is then assigned the value 5, which is an integer. The variable “a” is then assigned the value ‘Hello, World!’, which is a string. This results in a compilation error, because the variable “a” can only store integers. Note that code after “//” is considered a comment and won’t be executed.

```
1 int a; // Declare type as integer
2 a = 5;
3 a = 'Hello, World!'; // Compilation error!
```

Dynamic typing makes Python a very beginner-friendly language, since one does not have to keep track of the type of each variable. However, this also makes Python a slower language, because the interpreter has to check the type of each variable during code execution. Also, developing code with dynamic typing systems is prone to introducing bugs (“type errors”), because it allows unexperienced developers to convert variables from one type to another without noticing, leading to unexpected behavior. Hence, larger Python projects require disciplined adherence to programming conventions. One such convention is *type hinting*, which is a way to explicitly note the type of a variable. Type hinting does not have an effect on the code, but it makes the code more readable and understandable for other developers, and allows for development environments to detect type errors before execution (Listing 6) (van Rossum et al., 2014).

Listing 6: Example of type hints used in Python. Explicitly stating the type of the variable is optional and does not change the behavior of the code, but behaves exactly as shown in Listing 4.

```
1 a: int = 5
2 a: str = 'Hello, World!'
```

To make Python as easy as possible, python packages aim to reduce the amount of code that has to be written by the user. For example, the package `matplotlib` is a plotting library where every command is written such that the user immediately understands its purpose, like plotting a line or labeling an axis (Listing 7). Hence `matplotlib` code is a sequence of simple function calls, where the state of the plot is modified and saved in the background line by line.

However, when no pre-written functions or packages are available, Python offers the tools of a general purpose programming language to write and deploy custom code easily. Programming

Listing 7: Example of using pre-written functions of a Python package. The functions of the package `matplotlib.pyplot` become accessible by importing the package as `plt`, where `plt` serves as an alias (or rather shortcut) to access the functions of the package. Then, two arbitrary lists are defined, `x` and `y`. These datapoints are plotted (scatterplot) using the function `plot`. The plots x- and y-axes are then labeled and saved as an image. The code is written in a sequence of function calls, where the state of the plot is saved in the background. The plot is then displayed using the function `show`.

```

1 import matplotlib.pyplot as plt # Make functions accessible via plt
2 x = [1, 2, 3, 4, 5]             # Define arbitrary x values
3 y = [1, 4, 9, 16, 25]          # Define arbitrary y values
4 plt.plot(x, y)                 # Plot x against y
5 plt.xlabel('Timepoint')        # Add a label to the x axis
6 plt.ylabel('Foldchange')       # Add a label to the y axis
7 plt.title('Gene Expression')   # Add a title above the plot
8 plt.savefig('plot.png')        # Save plot as image onto harddrive
9 plt.show()                     # Show the plot preview

```

styles can be classified into two main paradigms: *functional* and *object-oriented* programming, which can be understood as different ways to structure code. Python supports both paradigms. In *functional* programming, the code is written in a way that the program is a sequence of function calls, where each function call returns a value that is used in the next function call (Listing 8). This approach is useful when multiple actions have to be performed on the same data and the structure of the data is relatively simple, for example a string of a gene sequence.

Listing 8: Example of functional programming in Python. The code defines a function called “`find_restriction_site`” that finds the position of a restriction site in a gene. The function “`cut`” uses the function “`find_restriction_site`” to cut the gene at the restriction site.

```

1 def find_restriction_site(gene: str): # Define a function
2     return gene.find('GCGC')         # Find the position of 'GCGC'
3
4 def cut(gene: str):                  # Define another function
5     position = find_restriction_site(gene) # Use the function above
6     return gene[position:]           # Cut the gene at the position
7
8 gene1 = 'TGAGCTGAGCTGATGCGCTATATTAGGCG' # Define an arbitrary gene
9 gene1_cut = cut(gene1)                # Cut the gene
10 print(gene1_cut)                     # Show the result
11 # Output: GCGCTATATTAGGCG

```

When the data itself gains in complexity, for example when storing not just the gene sequence, but also the promotor sequence, an *object-oriented* approach is more suitable (Listing 9). Object-oriented programming is a programming paradigm that uses objects and classes. An object is a collection of both data and functions, and a class is a blueprint for creating objects. The data of an object is stored as *attributes*. Functions that are associated with an object are called *methods*.

Listing 9: Example of object oriented programming in Python. The class is called “`Gene`” and has four methods, “`__init__`”, “`find_promotor`”, “`find_restriction_site`” and “`cut`”. The method “`__init__`” is called when creating (“initializing”) an object, which fills the object with user-defined data. The parameter “`self`” is used to reference the object itself internally. “`find_promotor`” is a method that finds the position of the promotor in the gene and is called during object initialization.

```

1 class Gene:                                # Define a Gene class
2     def __init__(self, sequence: str):      # Define how a Gene object is created
3         self.sequence: str = sequence      # Save sequence as attribute
4         self.promotor: str = self.find_promotor() # Automatically find promotor
5     def find_promotor(self):                # Define how to find the promotor
6         return self.sequence.find('TATA')
7     def find_restriction_site(self):        # Define how to find restriction site
8         return self.sequence.find('GCGC') # Find the position of 'GCGC'
9     def cut(self):                         # Define how to cut the gene
10        position = self.find_restriction_site() # Call the method above
11        return self.sequence[position:]    # Cut the gene at the position
12
13 gene1 = Gene(sequence='TGAGCTGAGCTGATGCGCTATATTTAGGCG') # Create Gene object
14 gene1_cut = gene1.cut()                    # Call the method cut
15 print(gene1_cut)                          # Show result
16 # Output: GCGCTATATTTAGGCG

```

A major benefit of using an object oriented versus a functional approach is that the data itself is programmable, enabling the programmer to define the behavior of the data itself through methods. This is achieved by using the keyword “self” to reference the object itself inside the class. For example, one could extend the class “Gene” with a method that finds the promotor of the gene and stores it as an attribute (Listing 9).

When designing software, both functional and object oriented programming can be used together, where object oriented programming is often used to design the program’s overall architecture, and functional programming is used to implement the algorithms of the program’s features. This allows for scalability of the software, as every single class is extended through the addition of new methods. Furthermore, classes can be expanded in their functionalities through *inheritance* (Listing 10). Inheritance is a feature of object-oriented programming that allows a class to access every attribute and method of a parent class. For example, one could extend the class “Gene” with a class “mRNA”, by writing a class “mRNA” that inherits from the class “Gene”.

Listing 10: Example of inheritance in Python. The class “mRNA” inherits from the class “Gene”. The class “mRNA” has two methods, “__init__” and “find_stopcodon”. The method “find_stopcodon” finds the position of stop codons.

```

1 class mRNA(Gene):                          # Define the mRNA class, inheriting from Gene class
2     def __init__(self, sequence: str):      # Define how an mRNA object is created
3         super().__init__(sequence)        # Get attributes from parent class
4         self.sequence.replace('T', 'U')   # Replace thymine with uracil
5     def find_stopcodons(self):             # Define how to find stop codons
6         return self.sequence.find('UGA') # Find the position of 'UGA'
7
8 mrna1 = mRNA(sequence='TGAGCTGAGCTGATGCGCTATATTTAGGCG') # Create mRNA object
9 print(mrna1.find_stopcodons())            # Show the position of stop codons
10 # Output: [0, 5, 10]

```

Together, Python is not just beginner-friendly, but also well respected for its ease in development, which is why it is widely used in professional settings for web development, data

analysis, machine learning, biosciences and more (Ekmekci et al., 2016; Rayhan & Gross, 2023).

The Potential of Python Data Science Packages for Biomedicine

Python includes a vast number of built-in packages used for basic data-types, software development, simple math operations, etc., (*The Python Language Reference*, 2024). Still, Python relies on packages developed by its users to provide specialized tools for data analysis. A Python package consists of multiple Python *modules*, where each module is a text-file with a `.py` ending containing Python code. Famous examples of such packages are `pytorch` and `tensorflow`, that are used to build models of artificial intelligence, including *ChatGPT* (Paszke et al., 2019; Abadi et al., 2016; Radford et al., 2019). Here, we outlay the most important packages used for `plotastic` in Chapter 2 and present examples how these packages are utilized in modern biomedical research.

Interactive Python: The standard Python interface is insufficient for data science, because it lacks the tools to quickly and conveniently visualize and explore data. IPython can be understood as an enhanced version of the standard Python interpreter, designed to improve the interactivity of Python code execution (Perez & Granger, 2007). IPython introduces features like rich media support to display graphics, but also helps users to use correct python data types through dynamic type introspection, detecting errors in the code. This functionality is akin to what *MATLAB* and *RStudio* provide through their advanced graphical user interfaces and extensive debugging tools. IPython is most often utilized in the form of *Jupyter Notebooks*.

Jupyter: Jupyter is an evolution of IPython, introducing the *Jupyter notebook* format, which has the file-ending `.ipynb` (Kluyver et al., 2016). Jupyter Notebooks are documents that combine both code and text structured as *code cells* and *markdown cells*, respectively. Markdown cells allow the author to provide additional information with text formatting, for example structuring the document with headings and subheadings, adding hyperlinks, images and mathematical formulas. Code cells can be executed individually, displaying the output directly below the cell. This allows for an interactive exploration of data, but also makes Jupyter Notebooks a very human-readable format that outlays data analysis in a clear manner with precise and reproducible documentation of all data processing steps. Another major benefit of Jupyter Notebooks are interchangeable *Kernels*, allowing the execution of code in different programming languages, such as R, Julia, and C++ (Giorgi et al., 2022). Today, Jupyter Notebooks have become a standard format compatible with collaborative platforms like *Google Colab* and *JupyterLab*, but also professional software development tools like *VS Code*, and *PyCharm*. For biomedical research, Jupyter Notebooks are a powerful solution for improving reproducibility: They elegantly combine both documentation and code execution into a concise presentation of the data analysis process, hence being an intuitive tool to both capture and

embed computational work directly into papers, a requirement postulated by Mesirov (2010). Jupyter notebooks are increasingly found in the supplemental of modern publications of both bioinformatics and wet-lab research (Taskiran et al., 2024; Bosch-Queralt et al., 2022; Howe & Chain, 2015).

NumPy: Central processing units (CPU) usually execute one instruction on one data point at a time. For manipulating tabular data, this is inefficient as the same instruction must be repeatedly loaded for every data point. NumPy accelerates the mathematical capabilities of Python by enabling large-scale operations on multi-dimensional arrays and matrices with high efficiency (Harris et al., 2020). One key feature of NumPy is the implementation of “vectorization” or SIMD (Single Instruction, Multiple Data) instructions. SIMD allows multiple data points to be processed simultaneously, significantly speeding up operations that are inherently parallelizable, such as matrix addition or multiplication. NumPy’s syntax and functional approach to array manipulation have set a standard for matrix computation, influencing the design of advanced AI frameworks such as PyTorch and mlx, which mirrors several of NumPy’s functionalities to facilitate ease of use for those familiar with NumPy (Paszke et al., 2019; Hannun et al., 2023). This standardization has made NumPy an attractive tool not only in genomics (Ding et al., 2023), but also for modern clinical applications like imaging technologies and augmented-reality in surgery (Thompson et al., 2020).

Pandas: Tables are the most common way to store experimental results. Pandas extends Python with a tabular datatype, called DataFrame, which allows for easy data manipulation with integrated indexing (McKinney, 2011). The intuitive interface of Pandas can be likened to *Microsoft Excel*; however, it is vastly more powerful due to its speed, functionality, and ability to handle larger datasets, e.g. by running efficient numpy vectorization in the background. Unlike *Excel*, Pandas enables automation by summarizing processing commands into scripts, documenting each step, and ensuring reproducibility. Pandas is used in biomedicine for data wrangling, data cleaning, and data analysis, as it allows for the integration of multiple data sources into a single table (Santos et al., 2020).

matplotlib: matplotlib is a plotting library that provides a wide range of static, animated, and interactive plots and graphs Listing 7 (Hunter, 2007). It serves as the foundation for many visualization tools and is particularly valued for its flexibility and customization options. For example, Pandas uses matplotlib to plot column datapoints directly from a DataFrame object, creating histograms or scatter plots, which is useful for preliminary data analysis and checking data distributions. However, matplotlib uses a low-level syntax, hence plots generated by matplotlib can be cumbersome to format and customize.

seaborn: While the low-level syntax of matplotlib is valued for its flexibility, formatting publication grade plots can be laborious, and its inconsistent syntax can make it difficult to

remember the correct commands for different plot types. `seaborn` is a high-level interface on top of `matplotlib` that offers a more intuitive and highly standardized syntax across a wide array of plot types (Waskom, 2021). `seaborn` also integrates closely with Pandas data structures: It automatically groups datapoints, calculates measures of both central tendency (e.g. mean, median) and variance (e.g. standard deviation), and displays them into the plot (e.g. error bars). This completely replaces manual calculation of descriptive statistics. `seaborn` also offers intuitive grouping (*facetting*) of data points, which simplifies the creation of complex visualizations involving multidimensional data, making it easier to reveal patterns and relationships via color encoding, faceting, and automated statistical fits. This is particularly useful in biomedical research for visualizing and understanding complex datasets, such as large quantities of protein data (Krzywinski & Savig, 2013; Weiss, 2022). `seaborn` could indirectly contribute to improving reproducibility in biomedical research by making visualizations of complex data very accessible through an easy and standardized syntax.

Pingouin: Integrating both data visualization and statistical analysis is beneficial for researchers who wish to conduct advanced statistical analysis without switching between different software environments. Pingouin is designed to be a user-friendly statistical tool that offers a straightforward syntax for performing statistical tests, which are commonly implemented in R (Vallat, 2018). Unlike R, Pingouin integrates seamlessly within the Python ecosystem, which allows combining data manipulation, analysis, and visualization all in one platform. This improves reproducibility by reducing the number of software tools required to analyze data. Despite its potential to streamline the data analysis process, Pingouin has not been widely adopted by biomedical research, yet. One example of a study that utilized Pingouin is the work of Kelly et al. (2023) in the field of Patient Public Involvement (PPI), producing an ethical matrix that allows for the inclusion of stakeholder opinion in medical research design. This lack of Pingouin’s adoption in biomedicine could be due to recent development and the dominance of R in the field. However, since Python offers multiple benefits over R in syntax, software development, runtime performance and integration with other tools (like including performant C++ code), Pingouin is an attractive standard for future statistical analyses in biomedicine (Gorelick & Ozsvald, 2020).

Together, these python packages form the backbone of modern data analysis in Python, often times combining software from different languages to accelerate certain features, while retaining the ease of use and readability that Python is known for. This is particularly advantageous in the field of biomedicine, where the requirements of modern data analysis are often complex and require a high degree of flexibility and customization.

Aims

This project defines these aims:

- Characterize the interaction between myeloma cells and mesenchymal stromal cells
- Develop methods
- Face the challenge of time-dependent cell adhesion through
- Provide tools to analyze multidimensional cell adhesion data

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Appendices

A Supplementary Data & Methods

A.1 Figures

A.2 Tables

A.3 Materials & Methods

B Documentation of `plotastic`