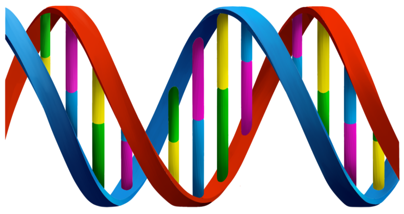
CS 46B Fall 2019
Homework 4
Curing cancer, one line of code at a time
Due 11:59 PM, Tuesday Oct 1, 2019



A major hope of modern medicine is to develop personalized treatment for cancer patients. This is already happening for a few kinds of cancer.

Every minute, around 40 million of our cells die and are replaced. The replacement cells come from healthy cells that divide into 2 identical copies that then grow to full size. Actually, the copies aren't perfectly identical. The DNA in the original cell contains 3 billion bases. (Bases are the small molecular subunits Adenine, Cytosine, Guanine, and Thymine, usually called by their abbreviations A, C, G, and T.) It's impossible to perfectly replicate 3 billion of *anything* and get it right every time. Sometimes there's an error, so that for example a thymine ("T") appears where a cytosine ("C") should be. Usually these errors, which are called *mutations*, do no harm, but sometimes they disrupt a part of the DNA that protects the cell against becoming a cancer cell. One cancer cell is not a threat, but then the cell divides, becoming 2, then 4, then 8, then 2^n neighboring cancerous cells: a tumor.

There are many different kinds of cancerous mutation. Often these different mutations respond to different kinds of treatment. Knowing the DNA sequence of the tumor cells of their patients gives doctors a huge advantage in prescribing therapy.

As you saw in lecture, patient care can begin with extracting DNA from a tumor, and determining its sequence using a machine that outputs a text file in "fastq" format. Unfortunately it is not yet possible to determine the ACGT… sequence of entire DNA molecules. The machine chops the molecule into lots of segments of a few hundred bases; these segments are called *reads*. We wish the fastq file could contain a single record with a very long sequence. Instead, until some hard technical problems are solved, fastq files contain thousands to millions of relatively short records.

The fastq file format, as you saw in lecture, has a group of 4 lines (a "record") for each read. The lines are:

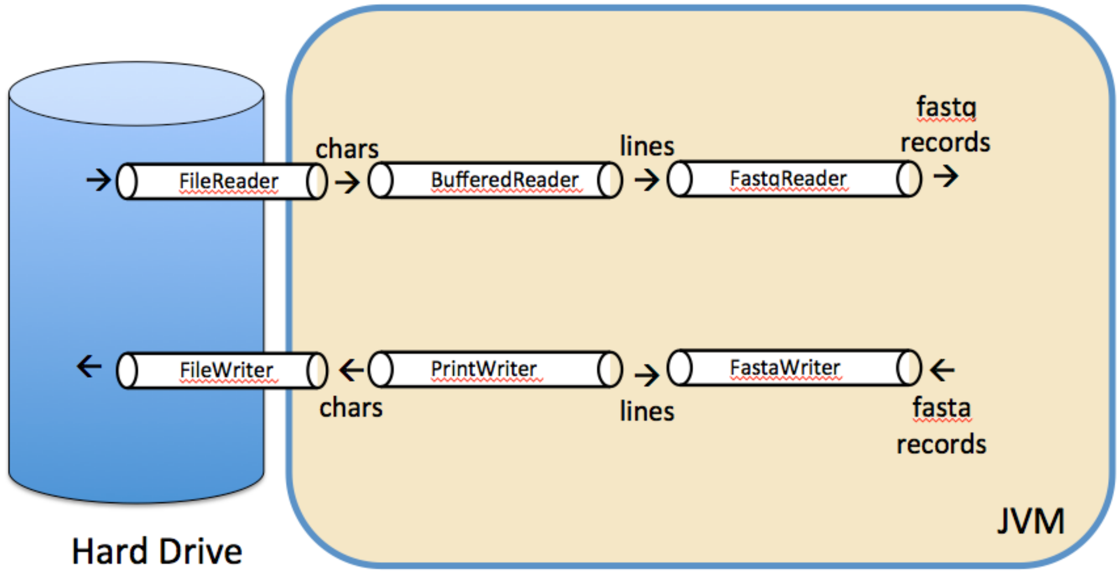
1) The “defline”: starts with @, followed by a unique identifier. All records in the fastq file are supposed to have different deflines. On rare occasions, a bug in the sequencer causes 2 or more records to have the same defline.
2) The sequence: a string of (usually) several hundred characters that represent the DNA sequence of the reads. The only legal characters (for this homework) are A, C, G, and T.
3) + (just a plus sign all alone on a line).
4) The quality. This is a string, exactly the same length as the sequence, of mysterious chars that encode the sequencing machine’s confidence that the corresponding char in the sequence is correct. The char representing minimum confidence is the exclamation mark (!).

You also saw that for bioinformatic analysis, fastq files are commonly converted into fasta format. A fasta file also has 1 record per read, but there are differences:

- Fasta files have only 2 lines per record: A defline and a sequence line.
- The defline starts with > rather than @.
- Fasta files have no quality information.

For this assignment you will write a Java app that reads a fastq file and creates a fasta file. Records in the fastq *might or might not* meet some quality threshold, and *might or might not* have unique deflines. Records in the fasta *must* all meet or exceed a quality threshold, and *must* all have unique deflines.

In class, you saw a method that almost does that, while reading from a BufferedReader and writing to a PrintWriter. For this assignment, you will use a different approach. You will create classes FastqReader (which will read from a BufferedReader) and FastaWriter (which will write to a PrintWriter).



In Eclipse, create a project called hw4, containing a package called dna, and import the 8 starter files that you downloaded with this assignment:

1) RecordFormatException.java
2) DNARecord.java
3) FastqRecord.java
4) FastaRecord.java
5) FastqReader.java
6) FastaWriter.java
7) FileConverter.java
8) DNAGrader.java

Then complete the starter files as described below. All classes, and all methods that you write, should be public.

Comments and Style

The comments in the starter files are instructions to you. After you finish the assignment, they aren't meaningful or relevant. So as you write each method, replace the starter comment with comments of your own that describe your code. Put a comment at the beginning of each class, at the beginning of most methods, and within methods if the method proceeds in several steps. For example, your convert() method will build its input stream, build its output stream, do the work, and then close its resources; each of those steps should start with a comment, and the steps should be separated by exactly 1 blank line.

The grader bot will give you 90 points for a perfectly working app. The remaining 10 points are for comments and coding style. Make sure your source code is neat and correctly indented. Make sure your variables have helpful names. Comment any class, method, or block of code within a method whose action isn't obvious.

When you run the bot, it will pop up a window for entering deductions for style and comments. That will be used by the human graders when they read your source code. Just click "OK" to see what grade you would get if you had perfect style and comments.

RecordFormatException.java

There is no starter file for this very simple class. It should extend Exception (*not* RuntimeException, because we want it to be checked). Provide one constructor whose arg is a String. Pass the String to the superclass constructor that takes a single String arg. This arg becomes the exception's message, and the exception handler can grab it by calling the exception instance's getMessage() method.

DNARecord.java

This interface doesn't need to be changed. Just read it and understand it.

FastqRecord.java

This class should implement DNARecord and should have:

- 3 String instance variables: defline, sequence, and quality.
- A constructor that initializes the instance variables. If the defline does not start with the correct character, the ctor should throw RecordFormatException with a helpful message. (If you're not sure how to get the 1st character of a string, check out the charAt(int) method of String on the API page.) Yes, ctors can throw exceptions just like methods; be sure to add "throws RecordFormatException" to the ctor declaration. Here are some possible messages, in increasing order of helpfulness:
    - An empty or null string
    - Zzup yo?
    - Oops
    - Bad fastq record
    - Bad defline in fastq record
    - Bad 1st char in defline in fastq record
    - Bad 1st char in defline in fastq record: saw X, expected @
- Methods that satisfy the DNARecord interface.
- An equals() method that checks for deep equality of all 3 instance variables.
- A boolean qualityIsLow() method that returns true if the quality contains at least one dollar sign ($) and at least one hash sign (#). If you don't know how to detect these conditions, look up the java.lang.String API. (In real life this method would be a lot more complicated.)
- A hashCode() method that returns the sum of the hash codes of defline, sequence, and quality.

FastaRecord.java

This class should implement DNARecord and should have:

- 2 String instance variables: defline and sequence.
- A constructor that takes 2 args – the defline and the sequence – and initializes the instance variables. As with FastqRecord, check to make sure the defline starts with the correct character (it's '>' for fasta records). Throw RecordFormatException if it doesn't.
- Another ctor with 1 arg – a FastqRecord – that initializes the instance variables with values from the FastqRecord. You'll have to change the 1st char of the defline. If you're not sure how to do this, look up the substring() methods on the String API page. This ctor shouldn't throw RecordFormatException.
- Methods that satisfy the DNARecord interface.

- An equals() method that checks for deep equality of the 2 instance variables.
- A hashCode() method that returns the sum of the hash codes of defline and sequence.

FastqReader.java

FastqReader should not extend any superclasses or implement any interfaces. It should have one instance variable: a BufferedReader named theBufferedReader.

This class should provide a single-arg ctor that initializes theBufferedReader from the ctor arg.

The class should also have the following method:

```
   public FastqRecord readRecord() throws IOException, RecordFormatException
```

This method should read a line from the buffered reader. If that line is null, the input file is at the end, and the method should return null. Otherwise the method should read 3 more lines and return a FastqRecord. The method should throw a RecordFormatException with a useful message if the 4 input lines don't constitute a valid fastq record. Note that this happens automatically if you call the FastqRecord ctor with invalid args; your code for this method shouldn't construct or throw anything.

FastaWriter.java

FastaWriter should not extend any superclasses or implement any interfaces. It should have one instance variable: a PrintWriter named thePrintWriter.

This class should provide a single-arg ctor that initializes thePrintWriter from its arg. The class should also have the following method:

```
   public void writeRecord(FastaRecord rec) throws IOException
```

This method should write the fasta record, in correct fasta format, to thePrintWriter.

FileConverter

This class should have 2 instance variables of type File, named fastq and fasta. Provide a ctor that has 2 File args and initializes the instance variables.

The class should have a convert() method and a main() method.

The convert() method should declare that it throws IOException. Any other exception types thrown in the body of convert() should be caught and handled inside convert(). The method should

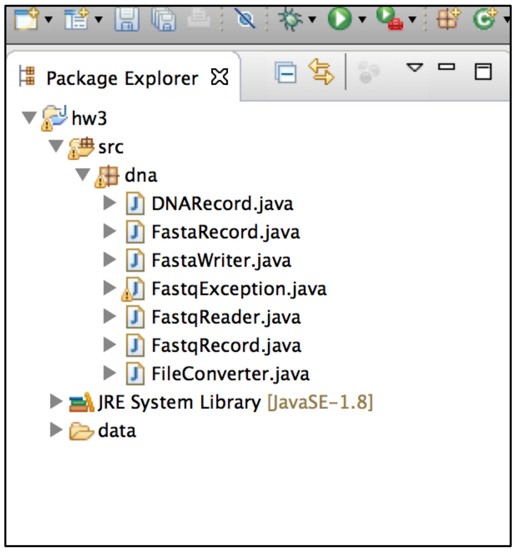
1) Create a FastqReader that reads from the fastq file specified by the fastq instance variable.
2) Create a FastaWriter that writes to the fasta file specified by the fasta instance variable.
3) Read each fastq record until the end of the fastq file is reached. Do nothing with any invalid records (i.e. records where the defline didn't start with @). For valid records where the quality isn't low, create a fasta record and write it using the FastaWriter.
4) Close all readers and writers that have close() methods, in reverse order of creation.

The main() method is provided for you. It reads and converts the fastq file that you downloaded with this assignment. The next section tells you what to do with the fastq file.

The Input File

Notice that the main() method reads a fastq file in a directory called data, and writes a fasta file in the same directory. You will need to create this directory in Eclipse, and import HW4.fastq into it.

To create the data directory, right-click on your project name in the package explorer and select New -> Folder in the popup menu. When prompted for the folder name, enter "data". You should see the new directory in the Package Explorer, at the same level as src. If it isn't at the right level, delete it and start again; it has to be in the right place for main() and the grader bot to find it.



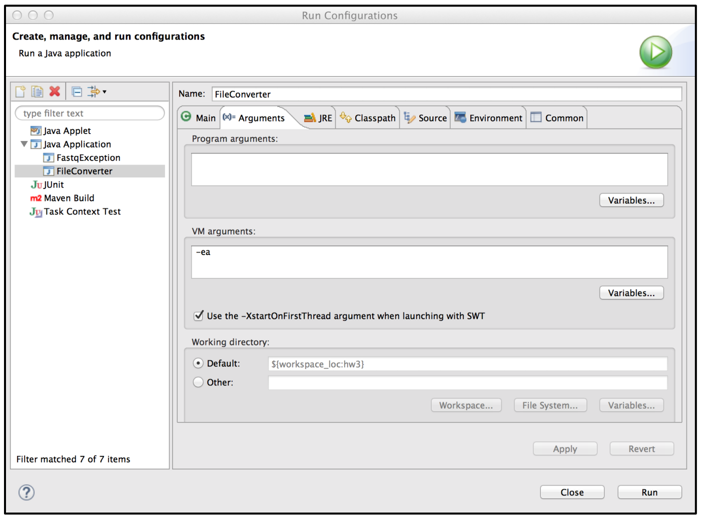
To import the fastq file, drag the icon for HW4.fastq into the icon of the data folder. A dialog box will ask you if you want to copy files or link to files; choose "copy files". Open the data folder by clicking on it; you should see HW4.fastq.

Testing

Run the app. If it runs correctly, it will create a file called HW4.fasta in the data folder. Unfortunately, when you do this the first time, you won't see HW4.fasta in the data folder. Eclipse doesn't know when an app writes a new data file. Right-click on the data icon and select Refresh in the popup menu. Now if you don't see HW4.fasta it's because something went wrong in your program.

Check your work. Double-click on the fastq file to open it. Look at the records and decide which ones are high-quality and valid. Then open the fasta file, and verify that it only contains fasta versions of the high-quality valid records.

You might want to use assertions to help develop your code. To enable assertions, select FileConverter in the Package Explorer. Go to the main Eclipse menu and select Run -> Run Configurations… Then click on the Arguments tab. Be sure that FileConverter is selected in the list on the left. If it isn't selected, select it there. Type –ea into the VM Arguments field (*not* the Program Arguments field) as shown below, and click Apply. Now when you run FileConverter as an app, "assert" statements will work.



Run Configurations

Create, manage, and run configurations

Run a Java application

Name: FileConverter

Program arguments:

VM arguments: -ea

✓ Use the -XstartOnFirstThread argument when launching with SWT

Working directory:

● Default: ${workspace_loc:hw3}

○ Other:

Filter matched 7 of 7 items

Run the DNAGrader app to see what your grade will be. The grader pops up a little window that the TAs will use to grade your comments and style. Just click the "ok" button. The Eclipse console will show your score, assuming no deduction for comments or style.

Submitting

As usual, export your project and upload. Use the jar command on the command line to be sure that your jar contains all your .java files. Don't submit HW4.fastq or HW4.fasta.

Late homework will not be accepted unless you have a documented emergency. Jar files that don't contain all the .java source files will receive zero points. Code that doesn't compile will receive zero points. This is not negotiable.

The Last Paragraph

This is the biggest assignment so far in 46B, and your code probably won't work right the first time. That's the way things are with realistic-size programs. Get comfortable with the process of figuring out what results you should see, and why you don't see them. START BY THINKING, NOT BY ASKING. You are here to develop your own skills at solving this kind of problem; debugging is part of the process, so you might as well enjoy it! (It's a lot less fun if you waited until the last minute to start the assignment.) Think about ways to insert temporary println statements, or use the debugger, or write a main() method that tests behavior of methods by passing very simple inputs. Or use "assert". For example, you could test FastqReader by creating a fastq file that contains one obviously correct record with a very short sequence, and putting println lines in readRecord() (or stepping through it with the debugger) to make sure the right thing happens. Then you can make the record invalid by changing @ to something else, and again seeing what happens. Delete your println statements after they are no longer useful.