UCR Dilution Framework

July 30, 2015

1 Dilution Framework

The Dilution Framework is a tool to create instructions for microfluidic technologies to dilute and compose composite chemical reagents. Additionally, it is designed for modularity so researchers can also easily implement their own dilution algorithms as well as compare and contrast previously implemented algorithms. Each algorithm outputs a mixing tree formatted as a directed acyclic graph (DAG) to be used by other applications. Source can be found at:

`https://github.com/UCRMicrofluidics/DilutionGenerator`

2 Algorithms

List of working algorithms in generator. A short description of each algorithm can be seen in section 4.

1. MinMix
   $< OutputCommandArguments >$ MINMIX CV_1 CV_2 ... $CName_1$ $CName_2$ ...
2. MTC
   $< OutputCommandArguments >$ MTC denominator $numerator_1$ $numerator_2$ ...
3. Remia
   $< OutputCommandArguments >$ REMIA numerator denominator
4. CoDos
   Priced Reageants:
   $< OutputCommandArguments >$ CODOS PRICED CV_{R1} Wt_{R1} CV_{R2} Wt_{R2} ...
   NON-Priced Reageants:
   $< OutputCommandArguments >$ CODOS CV_{R1} CV_{R2} ...
5. NRT_ISI
   $< OutputCommandArguments >$ NRT_ISI CV_1 CV_2 ...
6. Linear Gradient
   $< OutputCommandArguments >$ ISI_NCKU numerator denominator gradientStep numSteps
7. IDMA
   $< OutputCommandArguments >$ IDMA numOps tolerance desiredConcentration

8. DMRW
   $< OutputCommandArguments >$DMRW numOps tolerance desiredConcentration
9. Binary Search
   $< OutputCommandArguments >$ BINARYSEARCH numOps tolerance desiredConcentration

3 Output formats

There are several output options that can be chosen.

1. Digital Microfluidics Instructions
2. Continuous Flow Microfluidics Instructions
3. Dilution Generator File
4. DOT graph description language

Digital Microfluidics Instructions

These instructions format outputs the dag to be able to be consumed by a Digital Microfluidic system. MFSim is a digital microfluidics simulator developed by the Microfluidics lab at University of California, Riverside. You may download the simulator from

`http://microfluidics.cs.ucr.edu/staticsim.html`.

Continuous Flow Microfluidics Instructions

These instructions format outputs the dag to be able to be consumed by a Continuous Flow Microfluidic system. MCFlow is a continuous flow simulator that is being developed the Microfluidics lab at University of California, Riverside. This simulator is not publicly available at this time, but can be read about in the paper published by McDaniel here [6].

Dilution Generator File

This is a file that can be loaded into the UCR Dilution Framework. This allows work to be expanded, shared, or saved to be used later.

DOT graph description language

This is a file that can generate any file that reads DOT file formats. Further reading can found here `https://en.wikipedia.org/wiki/DOT_(graph_description_language)`.

3.1 Output Command Arguments

To specify the type of output you want, first specify the desired output type then the file name. To specify the console as output use "CONSOLE" as file name. Additionally the file name cannot have any spaces. To run use the following Commands:

DIGITAL FileName <Algorithm Command Line Arguments>
FLOW FileName <Algorithm Command Line Arguments>
DILUTGEN FileName <Algorithm Command Line Arguments>
DOT FileName <Algorithm Command Line Arguments>
ALL FileName <Algorithm Command Line Arguments>

4 Algorithm Descriptions

4.1 Min Mix

Inputs: Multiple Reagents
Outputs: Single Composite Reagent
Optimization: None

The concentration values(CV) must be integers. Although it is not required, for the most accurate output, the sum of the CVs should be divisible by powers of 2. Optionally, you may also specify the name (CName) for the concentration value that was passed in. MinMix is implemented as presented by Thies et al. [10]

4.2 MTC

Inputs: Single Reagent
Output: Multiple Diluted Reagents as specified.
Optimization: Minimum number mix-split steps to generate multiple diluent.

Inputs are the denominator and each numerator that is smaller than the denominator. The denominator **must** be divisible by power of 2. This algorithm follows the specification in Mitra et al. [7] The traveling salesmen problem is solved using the software available here: http://www.akira.ruc.dk/ keld/research/LKH/.

4.3 Remia

Inputs: Single Reagent
Output: Single Diluted Reagent
Optimization: Reactant Minimization

The inputs are the numerator and dominator for the final diluent. This algorithm follows the Remia implementation as specified by Huang et al. [4].

4.4 CODOS

Inputs: Multiple Reagents
Outputs: Single Composite Reagent
Optimization: Reactant Minimization, Price Minimization

The CVs for this algorithm must be integers. Additionally the sum of the CVs **must** be divisible by a power of 2. This algorithm also allows specification of price of the reagent. This algorithm follows the specification as presented in [5].

4.5 NRT_ISI

Inputs: Multiple CVs of the same reagent
Output: Multiple Diluted Reagents at desired CV.
Optimization: Optimized for Mix-Split steps and waste droplets.

The CV's need to add up to a power of 2 number. The implementation follow the specification in [1].

4.6 Linear Gradient

Inputs: Single Reagent
Output: Series of dilutes starting at the specified numerator.
Optimization: Optimized for Mix-Split steps and waste droplets for a linear series generation.

The denominator for this is algorithm must be a power of 2. This algorithm creates a series of diluted reagents starting at numerator and then outputting the every sample that is the difference apart. The implementation follows the specification from [2].

An example input of "100 256 3 5" would generate a mixing tree for: $\frac{100}{256}, \frac{103}{256}, \frac{106}{256}, \frac{109}{256}, \frac{112}{256}$.

4.7 IDMA

Inputs: Single Reagent
Output: Single Diluent
Optimization:

NumOps specifies the maximum number of operations(Mix-Split) steps that are allowed. The tolerance value bounds the rounding errors that occur from splitting droplets. The implementation follows the specification in [9]

4.8 DMRW

Inputs: Single Reagent
Output: Single Diluent
Optimization: Dilution and Mixing with Reduced Wastage

NumOps specifies the maximum number of operations(Mix-Split) steps that are allowed. The tolerance value bounds the rounding errors that occur from splitting droplets. The implementation follows the specification in [8]

4.9 Binary Search

Inputs: Single Reagent
Output: Single Diluent
Optimization:

NumOps specifies the maximum number of operations(Mix-Split) steps that are allowed. The tolerance value bounds the rounding errors that occur from splitting droplets. The implementation follows the specification in [3]

References

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[3] E. Griffith, S. Akella, and M. Goldberg. Performance Characterization of a Reconfigurable Planar-Array Digital Microfluidic System. *IEEE Transactions on Computer-Aided Design of Integrated Circuits and Systems*, 25(2):345–357, Feb. 2006.

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