Usage Guide for M3SYM v1.0

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1 Introduction

Cell motility plays a key role in human biology and disease, contributing ubiquitously to such important processes as embryonic development, wound repair and cancer metastasis. Papoian laboratory is interested in gaining deeper understanding of the physical chemistry behind these complex, far-from-equilibrium mechano-chemical processes. His approach and model, named *Mechano-chemical Dynamics of Active Networks, 3rd Generation* (MEDYAN3), is based on combining stochastic reaction-diffusion treatment of cellular biochemical processes with polymer physics of cytoskeletal filament network growth, while explicitly coupling chemistry and mechanics. For a more detailed description of MEDYAN3, please see (*paper here*)

Papoian laboratory has developed M3SYM, a software package based on the MEDYAN3 model, to simulate growth dynamics of actin based filamentous networks *in vitro* and *in vivo*. Recent papers where M3SYM or its predecessor, StochTools, were used can be found on the publication section of the Papoian group's main web page. The M3SYM package can also be extended to simulate the dynamics of any active matter network.

2 Overview of Features

M3SYM is a package that can simultaneously simulate complex chemical and mechanical dynamics of an active matter network. For more information on the MEDYAN3 model, which M3SYM implements, please see (*paper*)

2.1 Chemical capabilities

The chemical capabilities of M3SYM include:

- Stochastic reaction-diffusion on a three dimensional grid using stochastic simulation algorithms, including the *Gillespie* and *Next Reaction Method*.
- Complex chemical representation of filaments, allowing for heterogeneous chemical monomers in a single filament segment.
- A wide range of polymer reactions, including:
  - Polymerization of either end of filament
  - Depolymerization of either end of filament
  - Severing of filament at chosen sections
  - Branching of filament
  - Cross-linker binding and unbinding to filament

In the case of cytoskeletal networks, the following reactions can also be simulated:

  - Actin filament aging by ATP hydrolysis
  - Myosin IIA binding, unbinding, and walking

2.2 Mechanical capabilities

M3SYM allows for a wide range of mechanical interactions, including:

- Force fields for filament interactions, including
  - Filament stretching and bending
  - Branching point stretching and bending
  - Excluded volume interactions
- Stretching force fields for cross-linkers and motors
- Boundary interaction force fields

These force fields can be minimized by a choice of conjugate gradient algorithm.

2.3 Mechano-chemical coupling

M3SYM couples chemistry and mechanics by altering reaction rates based on mechanical stresses in a given network. This allows for a full treatment of the complex mechano-chemical responses in active matter networks. See (*paper*) for a more detailed description.

3 Running M3SYM

To run the M3SYM executable, put the following command into the terminal shell:

```
./M3SYM -s <SystemFile> -i <InputDirectory> -o <OutputDirectory>
```

The `SystemFile` will be described in the later sections.

The `InputDirectory` specifies where all input files are contained. This must be an absolute directory path. The `OutputDirectory` specifies where the produced output will be placed. This also must be an absolute directory path. See the later sections for details on input and output files.

4 Input

4.1 System file

The system file is a simple text file that defines all parameters of the simulation. The M3SYM executable must take in a system file as a command line argument.

Each parameter must be defined in the following syntax:

```
[PARAMETER]: [PARAMETERVALUE]
```

where the parameter name is followed by a semicolon, and the value of the parameter is placed after the semicolon. Outlined below are the parameters that can be included.

4.1.1 Geometry

The following geometry parameters can be set:

Parameter	**Value type**	**Description**
NDIM	1, 2, 3	Number of dimensions in system
NX	int	Number of compartments in X
NY	int	Number of compartments in Y
NZ	int	Number of compartments in Z
COMPARTMENTSIZEX	double	Size of compartment in X
COMPARTMENTSIZEY	double	Size of compartment in Y
COMPARTMENTSIZEZ	double	Size of compartment in Z
MONOMERSIZE	double	Size of monomer for filament growth
CYLINDERSIZE	double	Size of cylinder in filament
BOUNDARYSHAPE	SPHERICAL, CUBIC, CAPSULE	Boundary shape
BDIAMETER	double	Diameter for applicable shapes, including SPHERICAL and CAPSULE

4.1.2 Mechanics

The following mechanics parameters can be set. It should be noted that the number of parameters for each force field must match the number of chemical species of that type. Force field constant units are dependent on the potential used. For more information on force fields used, see (*paper*)

If a force field type is left blank, that force field will not be included in the simulation.

Parameter	**Value type**	**Description**
CONJUGATEGRADIENT	POLAKRIBIERE, FLETCHERRIEVES	Type of conjugate gradient minimization
GRADIENTTOLERANCE	double	Gradient tolerance in conjugate gradient
FSTRETCHINGTYPE	HARMONIC	Filament stretching force field
FSTRETCHINGK	double	Filament stretching force constant
FBENDINGTYPE	HARMONIC, COSINE	Filament bending force field
FBENDINGK	double	Filament bending force constant
FBENDINGTHETA	double	Filament bending angle
LSTRETCHINGTYPE	HARMONIC	Cross-linker stretching force field
LSTRETCHINGK	double	Cross-linker stretching force constant
MSTRETCHINGTYPE	HARMONIC	Motor stretching force field
MSTRETCHINGK	double	Motor stretching force constant
BRSTRETCHINGTYPE	HARMONIC	Branching point stretching force field
BRSTRETCHINGK	double	Branching point stretching force constant
BRBENDINGTYPE	COSINE	Branching point bending force field
BRBENDINGK	double	Branching point bending force constant
BRBENDINGTHETA	double	Branching point bending angle
BRDIHEDRALTYPE	COSINE	Branching point dihedral force field
BRDIHEDRALK	double	Branching point stretching force constant
BRPOSITIONTYPE	HARMONIC	Branching point position force field
BRPOSITIONK	double	Branching point position force constant
VOLUMETYPE	REPULSION	Volume force type
VOLUMECUTOFF	double	Volume interaction cutoff distance
VOLUMEK	double	Volume force constant
BOUNDARYTYPE	REPULSIONEXP, REPULSIONLJ	Boundary force type
BOUNDARYCUTOFF	double	Boundary interaction cutoff distance
BINTERACTIONK	double	Boundary force constant
BSCREENLENGTH	double	Boundary screening length constant

4.1.3 Chemistry

The following chemistry parameters can be set. It should be noted that the number of chemical species of each type must match the chemistry input file, as well as the number of mechanical parameters for each force field (if defined).

Parameter	**Value type**	**Description**
CHEMISTRYFILE	string	Input chemistry file. Should be in the `InputDirectory`
CALGORITHM	SIMPLEGILLESPIE, GILLESPIE, NRM	Chemistry algorithm used
NUMTOTALSTEPS	int	Number of total chemical steps to perform. If RUNTIME is set, this will not be used
RUNTIME	double	Total runtime of simulation (seconds)
NUMSTEPSPERS	int	Number of total steps per snapshot. If SNAPSHOTTIME is set, this will not be used
SNAPSHOTTIME	double	Time of each snapshot (seconds)
NUMCHEMSTEPS	int	Number of chemical steps per mechanical equilibration
NUMSTEPSPERN	int	Number of chemical steps per neighbor list update. This includes updating chemical reactions as well as force fields which rely on neighbor lists.
NUMDIFFUSINGSPECIES	int	Number of diffusing species in system
NUMBULKSPECIES	int	Number of bulk species in system
NUMFILAMENTSPECIES	int	Number of filament species in system
NUMPLUSENDSPECIES	int	Number of plus end species in system
NUMMINUSENDSPECIES	int	Number of minus end species in system
NUMBOUNDSPECIES	int	Number of bound species in system
NUMLINKERSPECIES	int	Number of linker species in system
NUMMOTORSPECIES	int	Number of motor species in system
NUMBRANCHERSPECIES	int	Number of brancher species in system
NUMBINDINGSITES	int	Number of binding sites per cylinder. This will set binding sites for cross-linkers, motors, and other binding molecules.

4.1.4 Dynamic rates

The following dynamic rate parameters can be set. These parameters are characteristic lengths of the rate changing equations outlined in (*paper*). These can be tuned to mimic the stall and unbinding forces of cross-linkers and motors.

Parameter	**Value type**	**Description**
FDPLENGTH	double	Characteristic length for filament polymerization rate change
MDULENGTH	double	Characteristic length for motor unbinding rate change
MDWLENGTH	double	Characteristic length for motor walking rate change
LDULENGTH	double	Characteristic length for cross-linker unbinding rate change

4.1.5 Output formats

The output of M3SYM will be directed to the `OutputFile` specified. The following output can be set. These outputs must be set on different lines, so users should specify a new OUTPUTTYPE parameter for each value desired. Output files will be explained in more detail in a later section.

Parameter	**Value type**	**Description**
OUTPUTTYPE	SNAPSHOT, FORCES, STRESSES, BIRTH TIMES	Output type