**Text S3. Implementation of the hybrid model of spontaneous cell polarization in VCell Math Workspace**

MathDescription {

Constant D 10.0;

Constant D1 0.1;

Constant D2 0.0;

Constant D3 0.1;

Constant k0 10.0;

Constant k1 0.01;

Constant k2 0.01;

Constant k3 0.01;

Constant k4 0.1;

Constant N 1000.0;

Constant tau 1.0;

Constant U\_init 1.0;

Constant S\_init 0.0;

VolumeVariable cell::U

MembraneVariable cell\_extra\_membrane::S

MembraneParticleVariable cell\_extra\_membrane::Gc

MembraneParticleVariable cell\_extra\_membrane::Go

Function flux ((Go \* k1 \* U) - (k2 \* S));

CompartmentSubDomain cell {

 BoundaryXm Flux

 BoundaryXp Flux

 BoundaryYm Flux

 BoundaryYp Flux

 BoundaryZm Flux

 BoundaryZp Flux

 PdeEquation U {

 Rate 0.0;

 Diffusion D;

 Initial U\_init;

 }

}

CompartmentSubDomain extra {

 BoundaryXm Flux

 BoundaryXp Flux

 BoundaryYm Flux

 BoundaryYp Flux

 BoundaryZm Flux

 BoundaryZp Flux

}

MembraneSubDomain cell extra {

 BoundaryXm Value

 BoundaryXp Value

 BoundaryYm Value

 BoundaryYp Value

 BoundaryZm Value

 BoundaryZp Value

 PdeEquation S {

 Rate (602.0 \* flux);

 Diffusion D3;

 Initial S\_init;

 }

 ParticleProperties Gc {

 ParticleInitialCount {

 ParticleCount N;

 ParticleLocationX u;

 ParticleLocationY u;

 ParticleLocationZ u;

 }

 ParticleDiffusion D1;

 }

 ParticleProperties Go {

 ParticleInitialCount {

 ParticleCount 0.0;

 ParticleLocationX u;

 ParticleLocationY u;

 ParticleLocationZ u;

 }

 ParticleDiffusion D2;

 }

 ParticleJumpProcess open {

 SelectedParticle Gc

 MacroscopicRateConstant ((k0 \* exp ((- t / tau))) + (k3 \* S));

 Effect Gc DestroyParticle

 Effect Go CreateParticle

 }

 ParticleJumpProcess close {

 SelectedParticle Go

 MacroscopicRateConstant k2;

 Effect Go DestroyParticle

 Effect Gc CreateParticle

 }

 JumpCondition U {

 InFlux - flux;

 OutFlux 0.0;

 }

}

}

Model geometry is introduced separately through a user interface:

 Domain: 3D, size= (8.4, 8.4, 8.4), origin= (0.0, 0.0, 0.0)

 Subdomains: “cell” ((x – 4.2) ^ 2.0 + (y – 4.2) ^ 2.0 + (z – 4.2) ^ 2.0) < (4.0 ^ 2.0);

 “extra” 1.0.