

# Appendix A

## Pseudo Code

In this appendix pseudo code for the GRN update algorithm of the xBioSys model, described in section 3.3, is presented.

Full source code is available at:

<http://panmental.de/ALifeXIflag/> (Development and Morphogenesis)

<http://panmental.de/motifs/> (Topological Network Analysis)

<http://panmental.de/GRNclocks/> and <http://panmental.de/CECDynAff/> (Dynamical Clocks and Differentiation)

### A.1 GRN Processing

```
//per time step
function process(){ //perfect matching version
//1. bind free proteins to matching cis sites
foreach GP : freeGPs{
    sharePerSite=GP.amount*bindingProportion/
                    sitesReceptiveFor(GP.type).length;
    foreach site : sitesReceptiveFor(GP.type)
        site.bind(sharePerSite);
    GP.addAmount(-(GP.amount*bindingProportion));
}
//2. call output function of genes and add output to free GP
foreach GP : freeGPs
    foreach gene : genes
        GP.addAmount(gene.getOutputFor(GP));
//3. saturation (upper bound) check
foreach GP : freeGPs
    if(GP.amount>saturationValue)
        GP.amount=saturationValue;
//4. decay free GP according to protein specific decay rate
foreach GP : freeGPs
    GP.amount=GP.amount*GP.proteinDecay;
```

```

//[5. output and input using scaling factor r]
}

function getBellCurveVal(double x, double sigma){
    return (1.0/sigma*root(2*PI))*exp(-((x*x)/(2*sigma*sigma)));
}

//...
function process(){ //smooth matching version
//1. bind free proteins to matching cis sites
foreach GP : freeGPs {
    shares=Array(n); //n is the number of bits for a GP
    shareSum=0.0;
    for(x=0;x<shares.length;x++){
        shares[x]=getBellCurveVal(x,0.5+GP.specificityFactor);
        shareSum+=shares[x];
    }
    for(int x=0;x<shares.length;x++) //normalize
        shares[x]/=shareSum;
    for(prot=0;prot<freeGPs.length;prot++){
        dis=getHammingDistance(toBinary(GP.type),toBinary(prot));
        share=shares[dis];
        switch(dis){
            case 0: num=1.0; break; //only one perfect match, i.e. type==prot
                //... how many proteins have hamming distance dis, up to n bits
            case n: num=1.0; break; //one differs in all three bits
        }
        amountForAllWithThisDis=(GP.amount*bindingProportion)*share;
        foreach site : sitesReceptiveFor(GP.type)
            site.bind(amountForAllWithThisDis/num/
                sitesReceptiveFor(GP.type).length);
    }
    GP.amount--=(GP.amount*bindingProportion);
}
}
//2. (see above)...

```

## A.2 Gene Processing

```

function tanhScaled(x, range, floor, rshift, slope){
//floorScale is added at the end to shift the whole 's' curve up.
floorScale = floor + (range/2);
//By reducing value of x, the whole 'S' is shifted right.
x = x - rshift;
return ( ((exp(x/slope) - exp(-x/slope)) / 2) /
    ((exp(x/slope) + exp(-x/slope)) / 2)
    )
    * (range/2)
    ) + floorScale;
}

public double getOutputFor(GP){
if(GP.type!=this.type)
    return 0;
activation=0;
foreach cisModule : cisModules {
    if(cisModule.bindingSites.length==0)
        continue;
    temp=999999.0;
    foreach bindingSite : cisModule.bindingSites {
        if(bindingSite<temp)
            temp=bindingSite;
    }
}
}

```

```
        bindingSite*=GP.proteinDecay; //decay bound GP
    }
    if(cisModule.regulationMode) //inhibitory
        activation-=temp;
    else //ativatory
        activation+=temp;
    }
    if(expressionType) //default 'off' gene
        shift=15.0;
    else //default 'on' gene
        shift=-5.0;
    return tanhScaled(activation,150,0.0,shift,5);
}
```

## Appendix B

### Further Reading

In parts, the research presented in this book is based on earlier publications, including my PhD thesis, a book chapter, two journal, and six publications in conference proceedings.

- Knabe, J. F., Wegner, K., Nehaniv, C. L. and Schilstra, M. J. Genetic Algorithms and Their Application to In Silico Evolution of Genetic Regulatory Networks. In Fenyo, D (ed) *Computational Biology*, Vol. 673, pages 297-321, Humana Press, 2010.
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