Each IL activates multiple STATs [50 cytokines activate 7 stats]

Old Model New Model

```
STAT5 (S_5)
 IL-2
             STAT5 (S_5)
 IL-15
IL-12
             STAT4 (S_4)
IL-18
            NFKb (S_h)
 IL-21
            STAT3 (S_3)
IL-2
            500 U/ml
IL-15
             20 ng/ml
IL-12
             10 ng/ml
IL-18
             50 ng/ml
IL-21
             25 ng/ml
```

```
IL-2 STAT5 (S_5), STAT3(S_3), STAT1(S_1), STAT4 (S_4), NFKb (S_b) IL-15 STAT4 (S_4) IL-12 STAT4 (S_4) IL-18 NFKb (S_b), STAT3 (S_3), STAT1(S_1),
```

How to choose the right model?

```
Index I=IL2 n=IL21 m=IL18
                                                                                                                                                                                                                I=3
                                                                                                                                                                                                                                                                                                                                                                                                                               m=2
        9 3 1 1
10 3 1 2
                                                                                                                                                                                                             I=6,9,10
        11 3 2 1
12 3 2 2
                                                                                                                                                                                                              I=12,13,14
                                                                                                                                                                                                                 I=16
   22 6 1 2
23 6 2 1
24 6 2 2
25 7 1 1
     31 8 2 1

32 8 2 2

33 9 1 1

34 9 1 2

35 9 2 1

36 9 2 2

37 10 1 1

38 10 1 2

39 10 2 1

40 10 2 2

41 11 1 1

      44
      11
      2
      2

      45
      12
      1
      1

      46
      12
      1
      2

      47
      12
      2
      1

      48
      12
      2
      2

      49
      13
      1
      1

      50
      13
      1
      2

      51
      13
      2
      1

      52
      13
      2
      2

      53
      14
      1
      1

      54
      14
      1
      2

      55
      14
      2
      1

      56
      14
      2
      2

      57
      15
      1
      1

      58
      15
      1
      2

      59
      15
      2
      1

      60
      15
      2
      2

      61
      16
      1
      1

      62
      16
      1
      2

      63
      16
      2
      1

      64
      16
      2
      2
```

64 16 2 2

Assuing that IL2 can have 16 possibilities

1.	S5
2.	S5,S1
3.	S5, S3
4.	S5, S4
5.	S5,Sb
6.	S5,S3,S1
7.	S5,S4,S1
8.	S5,Sb,S1
9.	S5,S4,S3
10.	S5,S3,Sb
11.	S5,S4,Sb
12.	S5,S4,S3,S1
13.	S5,S3,S1,Sb
14.	S5,S4,S3,Sb
15.	S5,S4,S1,Sb
16.	\$5,\$4,\$1,\$b,\$3

64 possible Models to choose correct model

```
STAT5 (S_5), STAT3(S_3), STAT1(S_1), STAT4 (S_4), NFKb (S_b)
                                                         IL-2
                                                         IL-15
                                                                    STAT5 (S_5)
IL2 has 16 possibilities (I)
                                                                    STAT4 (S_4)
                                                         IL-12
                                                                    NFKb (S_b), STAT3 (S_3)
                                                          IL-18
             S5
1.
2.
            S5,S1
                                                          IL-21
                                                                    STAT3 (S_3), STAT1(S_1),
           S5, S3
3.
           S5, S4
4.
5.
           S5,Sb
                                IL21 (possibilities) (n)
                                                               IL18 (possibilities) (m)
6.
          (S5,S3,S1)
                                           S3
                                1.
                                                               1.
                                                                           Sb
          S5,S4,S1
                                                                         (Sb,S3)
                               2.
                                                               2.
                                         S3,S1
8.
          $5,$b,$1
         S5,S4,S3
9.
         S5,S3,Sb
10.
11.
          $5,$4,$b
                                   IL15 (possibilities)
                                                                 IL12 (possibilities)
12.
        S5,S4,S3,S1
                                            S5
                                                                           S4
                                   1.
        S5,S3,S1,Sb
13.
14.
        S5,S4,S3,Sb
15.
        S5,S4,S1,Sb
      (S5,S4,S1,Sb,S3)
16.
                                                                       16 X 2 X 2X 1 X 1=64 models
```