Introduction to MapMaker and Creating a Linkage Map

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Purpose

- Show how to download, install, and run MapMaker 3.0b

- Show how to properly format a data set for loading into MapMaker

- Show how to use MapMaker to create a basic linkage map using an example F_2 population

Additional Notes

- It is important to note that there are numerous other powerful commands in MapMaker that I have not described here. The 'help' command in MapMaker shows the list of all commands and provides details on what each does. The commands shown here are the simplest commands needed to learn to use MapMaker and to create a linkage map using straightforward data.

- The data set in this example was simple and it was therefore easier to map. More complicated or different data sets can take days to map and can take a great deal of effort to test multiple map possibilities.

Linkage Map

- "A linkage map is a genetic map of a species or experimental population that shows the position of its known genes or genetic markers relative to each other in terms of recombination frequency, rather than as specific physical distance along each chromosome"

  - Wikipedia

- Centimorgan (cM) – unit of recombinant frequency equal to a 1% chance that one marker will be separated from another marker due to cross over in a single generation

  -Wikipedia

MapMaker

- Created by Stephen Lincoln, Mark Daly, and Eric Lander at Massachusetts Institute of Technology (1987)
- Version 3.0b came out in January 1993 (current version)
- Creates genetic linkage maps of a given population using markers
  - Uses lowest log-likelihood to create most likely sequence that would give rise to observed marker data
- MapMaker allows manual trial and error
- F_2 intercrosses, F_2 backcrosses, F_3 intercrosses, Recombinant inbred lines (RILs)
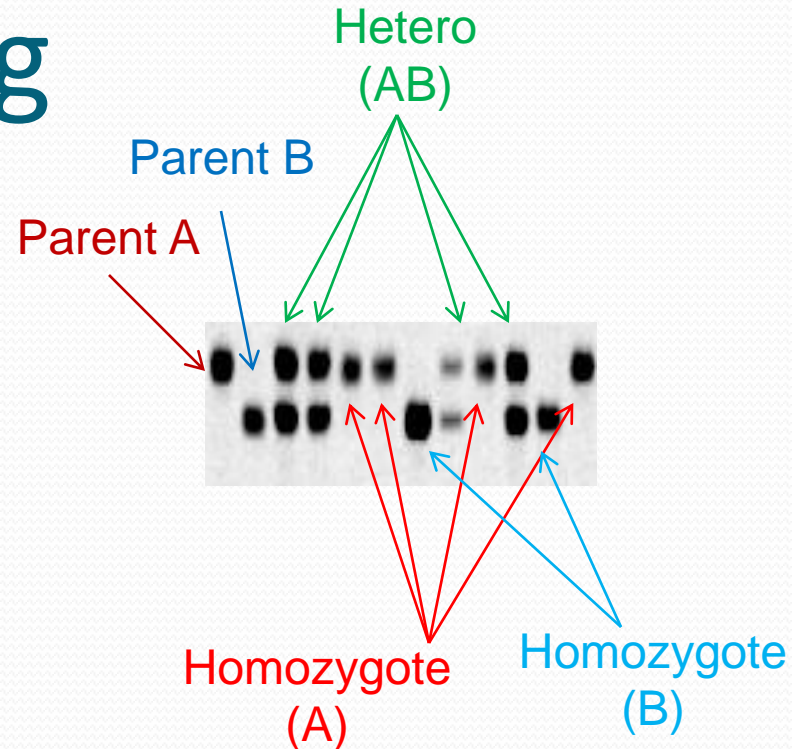- Another brief tutorial is available at http://linkage.rockefeller.edu/soft/mapmaker/

Installing

- MapMaker/EXP 3.0b is available for free at http://www.broadinstitute.org/ftp/distribution/software/mapmaker3/
  - Download all 18 files to a folder in the root directory you wish to use (typically c:\mapmaker\)
    - Install as close to root directory as possible – some errors occur when installed nested in folders
    - Includes two read me's: one for installing and one for using MapMaker
  - Run the two exe files (mapm3pc1.exe and mapm3pc2.exe)
    - This can be done in Windows
- MapMaker runs in DOS only
  - Although all versions of Windows have command prompt, newer versions often lock up and crash when running MapMaker
  - Highly recommended to use a DOS emulator to run on any current operating system (Mac or PC)
    - DOSBox 0.73 is available for free at http://www.dosbox.com/download.php?main=1
    - (OS X, Windows, OS/2 and others)

Data

- Data must be formatted in a specific way or MapMaker will not be able to recognize it
- MapMaker has defaults for what thresholds to use as well as what scoring system is used
  - These can be changed to virtually anything you may want to try
    - For this tutorial, I will show how to use a different scoring system than the default
- MapMaker will typically tell you if there is an error in the formatting of the data and how to fix it
  - Example – marker names cannot contain "/"
    - EP1564/1565 must be formatted as just EP1564

Scoring

- MapMaker Standard Scoring
  - A = Parent A
  - B = Parent B
  - H = Heterozygote
  - C = Not a homozygote for allele A (either BB or AB)
  - D = Not a homozygote for allele B (either AA or AB)
  - "-" = Missing value
- Can substitute any symbol/system you choose, just have to tell MapMaker what each symbol equals

Formatting of Data in Excel

- Recommend making data table in Excel
  - Two sheets – one has all data and marker info you wish to record, the other will have the correctly formatted data for MapMaker
- General Data Sheet
  - Important to review your data
    - Too much missing data
    - Unexpected segregation
- MapMaker Sheet
  - Special Header – different for each type of population
    - F2 intercross, F2 backcross, F3 self, RI self, RI sib
  - First column contains marker names - must put an asterisk (*) before each marker name, this allows MapMaker to recognize it as the marker name
  - Do not include parents or any other data (such as segregation or missing data statistics)
- Save as a tab delimited txt file
  - Must be saved in the same folder as MapMaker program

Example Data Set

- Data is from an F_2 cross between *Solanum lycopersicum* cv 'VF36' and *Solanum pennellii* LA716 (wild species)

- 104 individuals

- Standard A,B,H,C,D scoring system was not used
  - In this case, 1=A, 2=H, 3=B, 4=C, 5=D, and -=-

- Example data created with the help of Reynaldo Nuñez Salazar, Jennifer Moyseenko, and Esther van der Knaap

Text file exported from Excel (tab delimited)

Note: see included example files for whole document

Starting

- Open DOS emulator program
  - If using DOSBox, you must mount the drive MapMaker is located on – to do this simply use the following set of commands
    - mount c c:\
    - c:\
    - cd mapmaker
    - mapmaker
  - This will start MapMaker
  - Note: if MapMaker is installed on a different drive, simply use the correct drive letter and folder name
    - Both DOSBox and MapMaker can be run from a flash drive

```
DOSBox 0.73, Cpu Cycles:    3000, Frameskip 0, Program:   DOSBOX
```

Welcome to DOSBox v0.73

For a short introduction for new users type: INTRO
For supported shell commands type: HELP

If you want more speed, try ctrl-F8 and ctrl-F12.
To activate the keymapper ctrl-F1.
For more information read the README file in the DOSBox directory.

HAVE FUN!
The DOSBox Team http://www.dosbox.com

```
Z:\>SET BLASTER=A220 I7 D1 H5 T6

Z:\>mount c c:\
Mounting c:\ is NOT recommended. Please mount a (sub)directory next time.
Drive C is mounted as local directory c:\

Z:\>c:

C:\>cd mapmaker

C:\MAPMAKER>
```

```
****************************************************************************
*  Welcome to:                                                            *
*                                                                         *
*                          MAPMAKER/EXP                                   *
*                          (version 3.0b)                                 *
*                                                                         *
*    Copyright 1987-1992, Whitehead Institute for Biomedical Research     *
****************************************************************************


Type 'help' for help.
Type 'about' for license, non-warranty, and support information.

1>
```

Initial Commands in MapMaker

- prepare example.txt
  - File must be located in MapMaker folder
  - If there are errors, MapMaker will tell you
    - Empty cells, marker name missing asterisk, inconsistent value for number of markers or individuals
- photo example.out
  - Can be any name – can use same data multiple times and create different output files for each "run"
  - Will save in MapMaker folder
  - Output file is always one command behind (aka current command is not saved until another command is run)
  - Read-only until you quit MapMaker
    - Opens in Microsoft Word
- **Vital to have out file – otherwise you will lose everything if MapMaker gets closed or crashes**

Basic Commands to create linkage map

- seq all
  - Sequences all markers
- group
  - Identifies groups of markers in last set
- seq # # # # #
  - Sequences specific markers (# = marker number)
- seq group1
  - Sequences a group from the last command results
- Order
  - Creates an order for the currently sequenced markers
- three point
  - Tests all possible orders of last set in groups of three
- map
  - Gives linkage map for last sequence (in cM)
- try #
  - tries to fit a marker into the last sequence (# = marker number)
- help
  - Provides list of all possible commands and brief description

'seq' & 'group' command

```
DOSBox 0.73, Cpu Cycles:     max, Frameskip  0, Program:   DOS4GW

map data in file 'EXAMPLE.MAP' is old... not loading
two-point data in file 'EXAMPLE.2PT' is old... not loading
unable to run file 'EXAMPLE.PRE'... skipping initialization
saving genotype data in file 'EXAMPLE.DAT'...   EXAMPLE.DAT
    1 File(s) copied.
 EXAMPLE.TMP
    1 File(s) copied.
ok
saving map data in file 'EXAMPLE.MAP'...   EXAMPLE.MAP
    1 File(s) copied.
 EXAMPLE.TMP
    1 File(s) copied.
ok

2> seq all
sequence #1= all

3>     group
Linkage Groups at min LOD 3.00, max Distance 50.0

group1= 1 2 3 8 10 11 12 13 14 15 16 18 20 24
-------
group2= 4 5 6 7 9 17 19 21 22 23 25 26 27

4> _
```

'map' command


```
other1= 10 15 8
=================================================================

7> seq order1
sequence #3= order1

8> map
=================================================================

Map:
  Markers         Distance
    2   ssr103     101.2 cM
   18   ssr57       20.6 cM
   14   ssr40       25.6 cM
   24   ssr96       12.4 cM
   13   ssr356       7.3 cM
   12   ssr349       3.5 cM
   20   ssr605      17.8 cM
   16   ssr50       16.7 cM
   11   ssr32       20.9 cM
    3   ssr125      42.4 cM
    1   ep1762     ----------
                   268.4 cM    11 markers    log-likelihood= -336.95
=================================================================

9> _
```
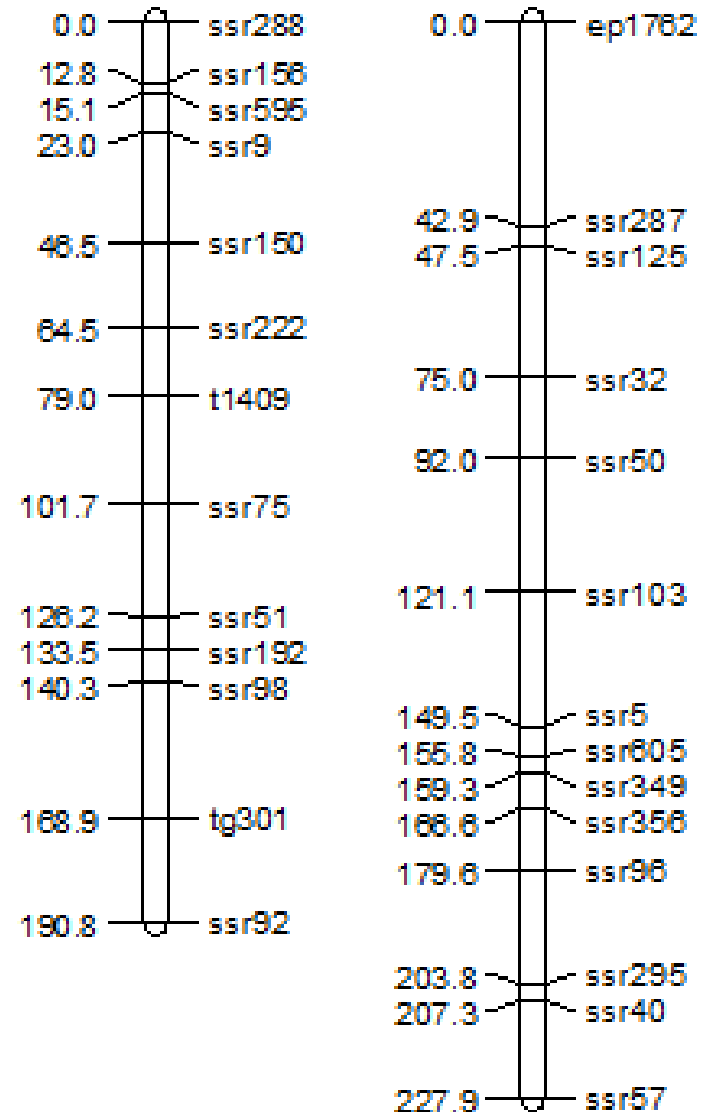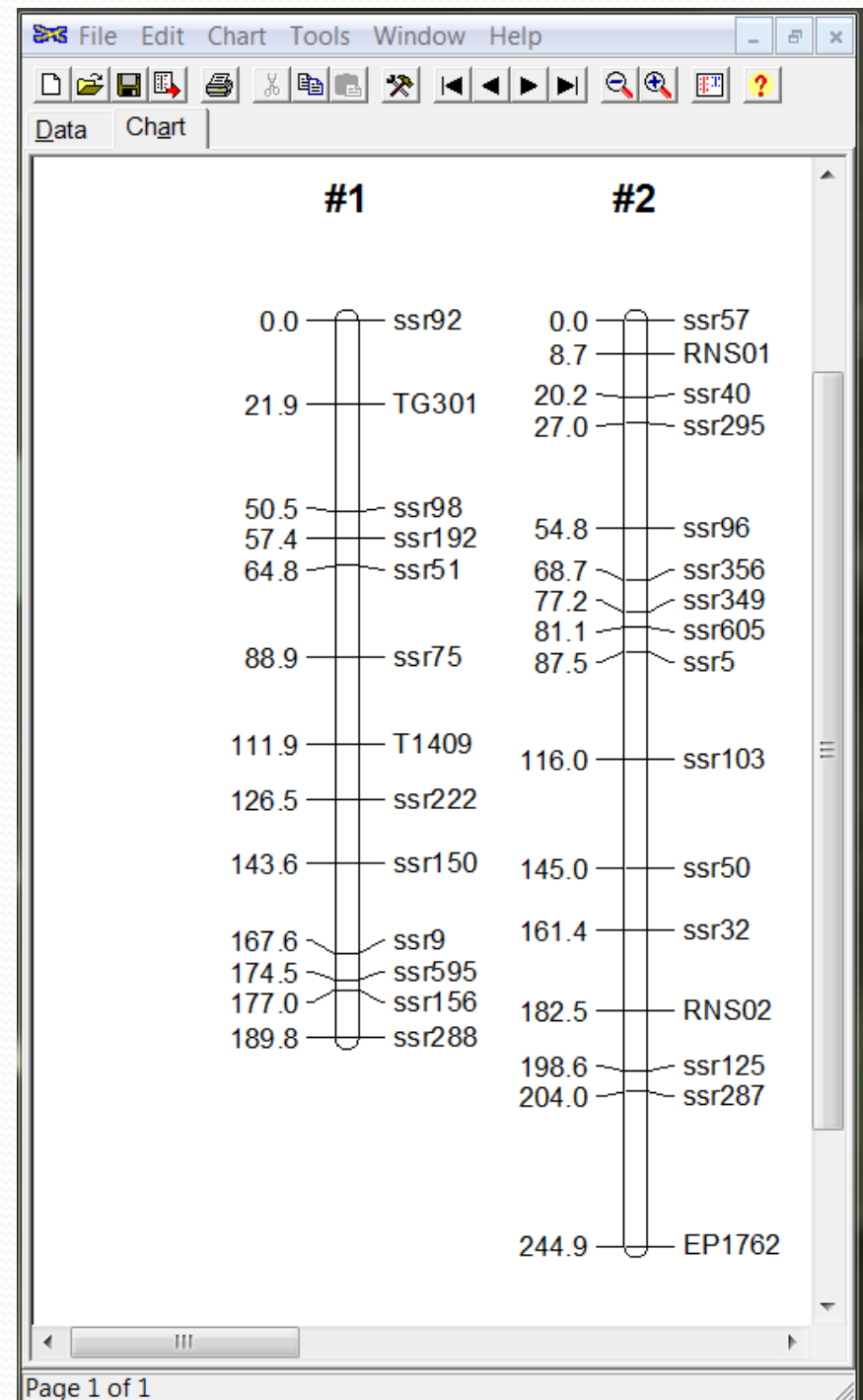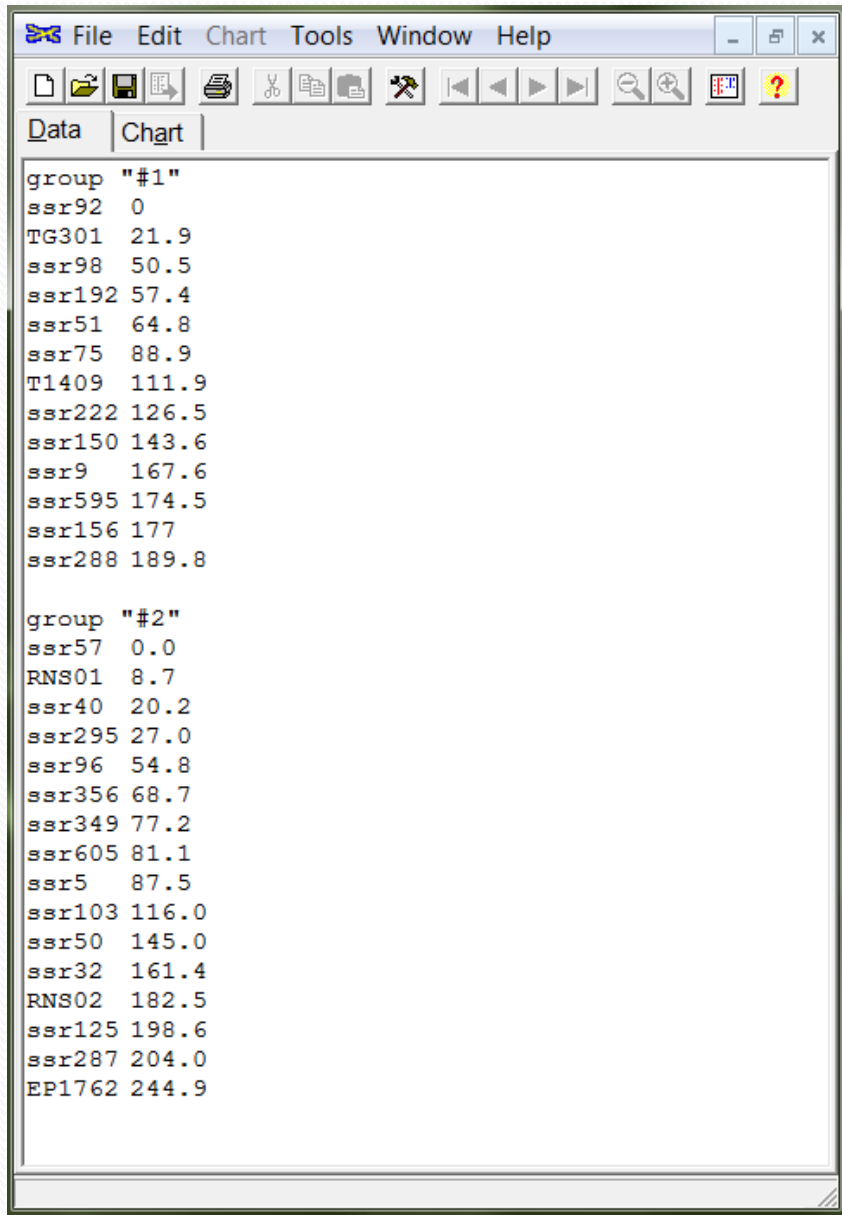
Output

- Can use MapChart 2.2 to create a visual map (available for free at www.biometris.wur.nl/uk/Software/MapChart/)

MapChart 2.2

External Links

Centimorgan [Online]. Wikipedia. Available at:
en.wikipedia.org/wiki/Centimorgan (verified 2 Dec 2010).

DOSBox [Online]. DOSBox. Available at: www.dosbox.com/download.php
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en.wikipedia.org/wiki/Genetic_linkage#Linkage_map (verified 2 Dec 2010).

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2010).

Lander, E. Mapmaker/EXP 3.0 Manual [Online]. Whitehead institute for
biomedical research. Available at: linkage.rockefeller.edu/soft/mapmaker/
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Mapchart [Online]. Wageningen University. Available at:
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Reference

Lander, E. S., P. Green, J. Abrahamson, A. Barlow, M. J. Daly, S. E. Lincoln,
and L. Newburg. 1987. MAPMAKER: an interactive computer package for
constructing primary genetic linkage maps of experimental populations.
Genomics 1:174-181.