From Arabidopsis roots to bilinear equations

Dustin Cartwright [1]

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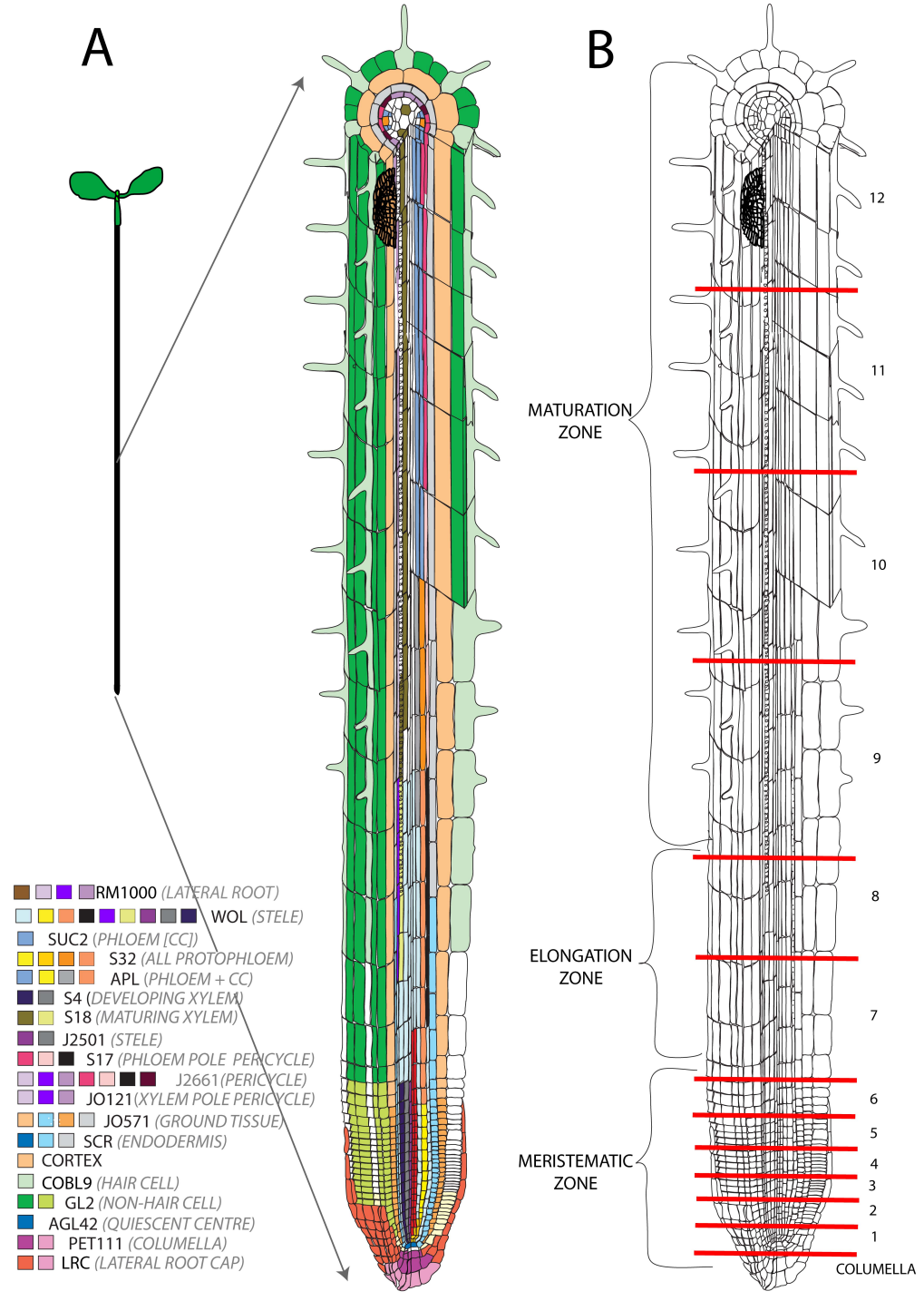
[1] joint with Philip Benfey, Siobhan Brady, David Orlando (Duke University) and Bernd Sturmfels (UC Berkeley), research supported by the DARPA project Fundamental Laws of Biology

Arabidopsis root



Arabidopsis root

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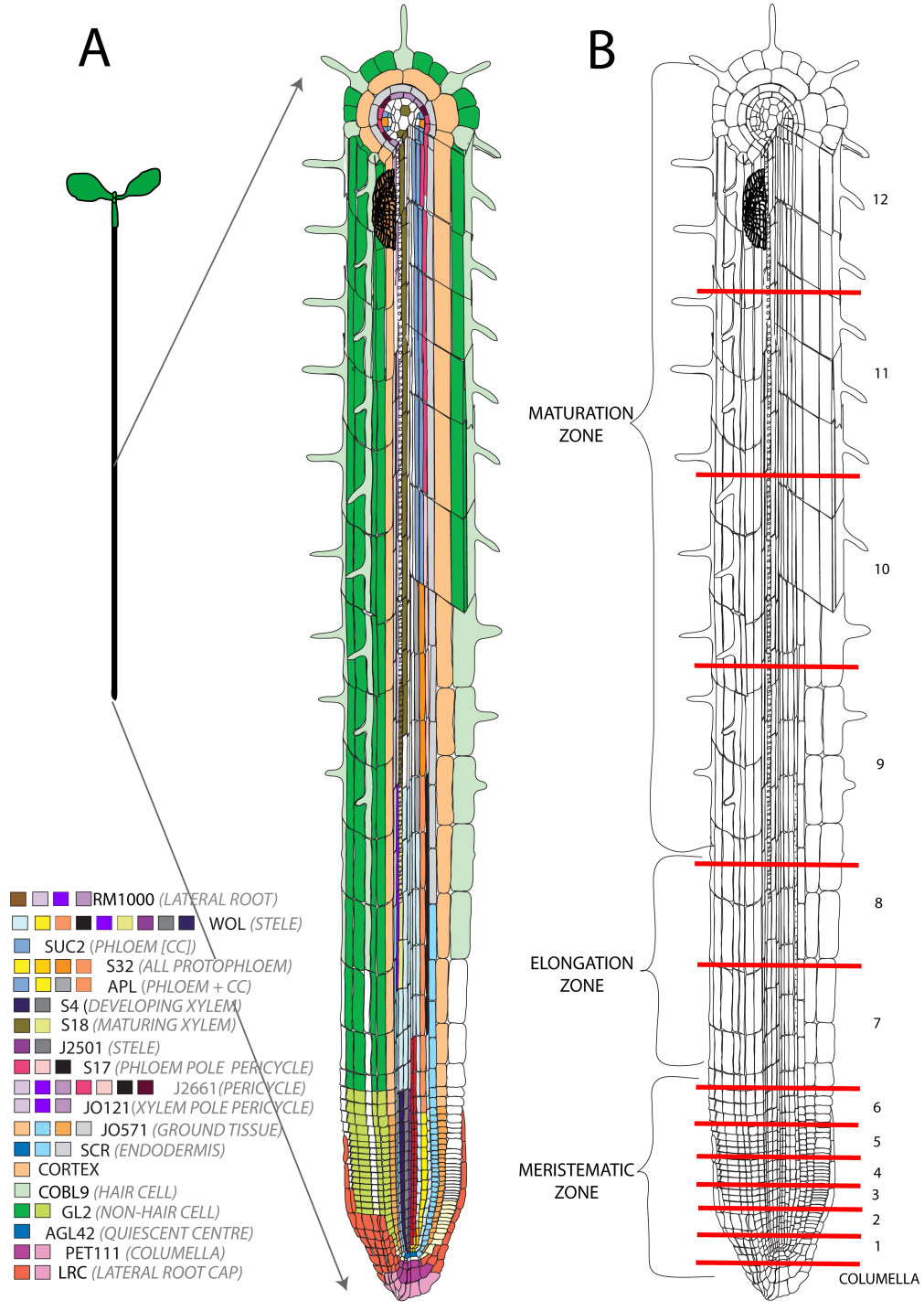

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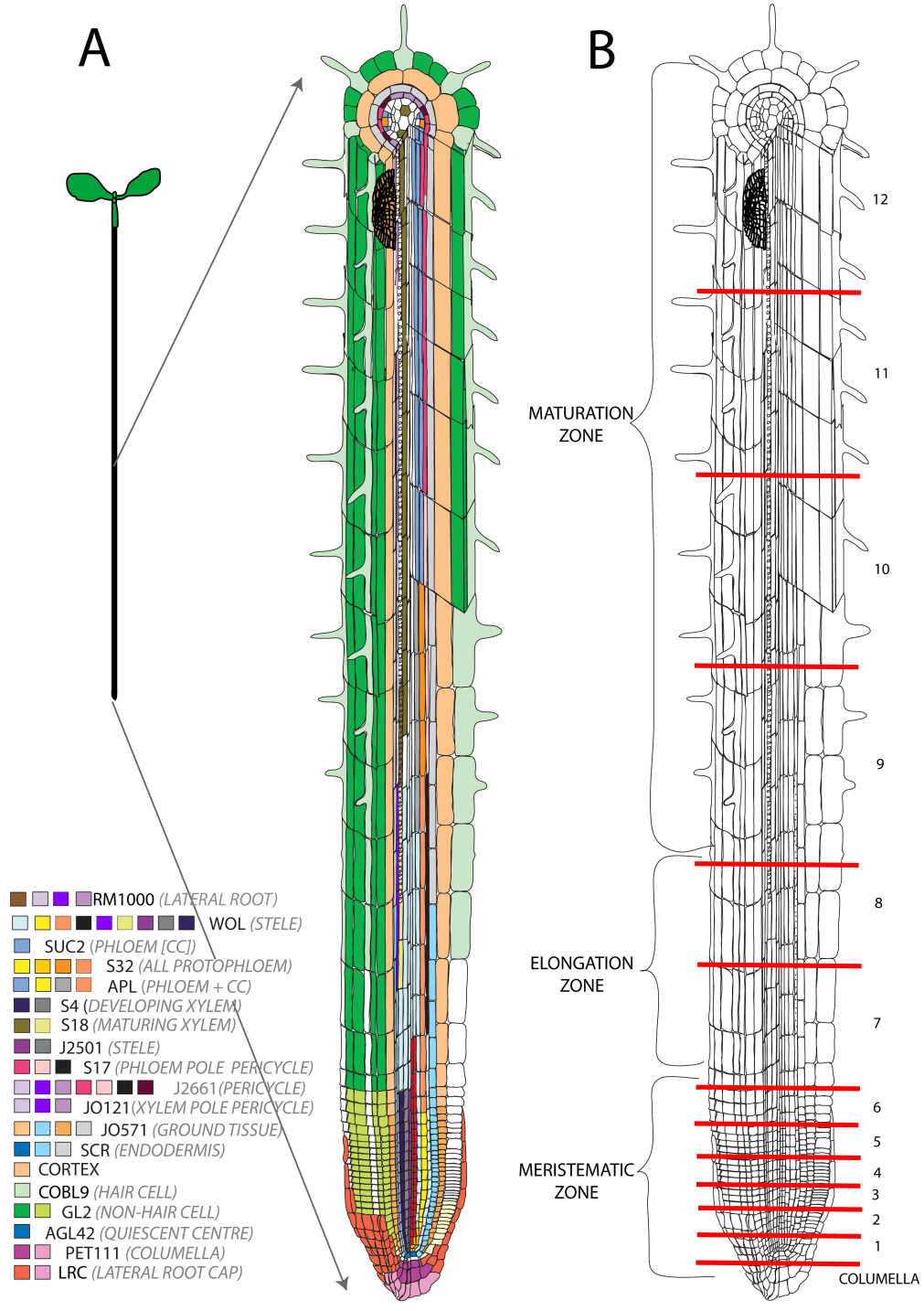
- Chemically, using 18 markers (colors in diagram A)



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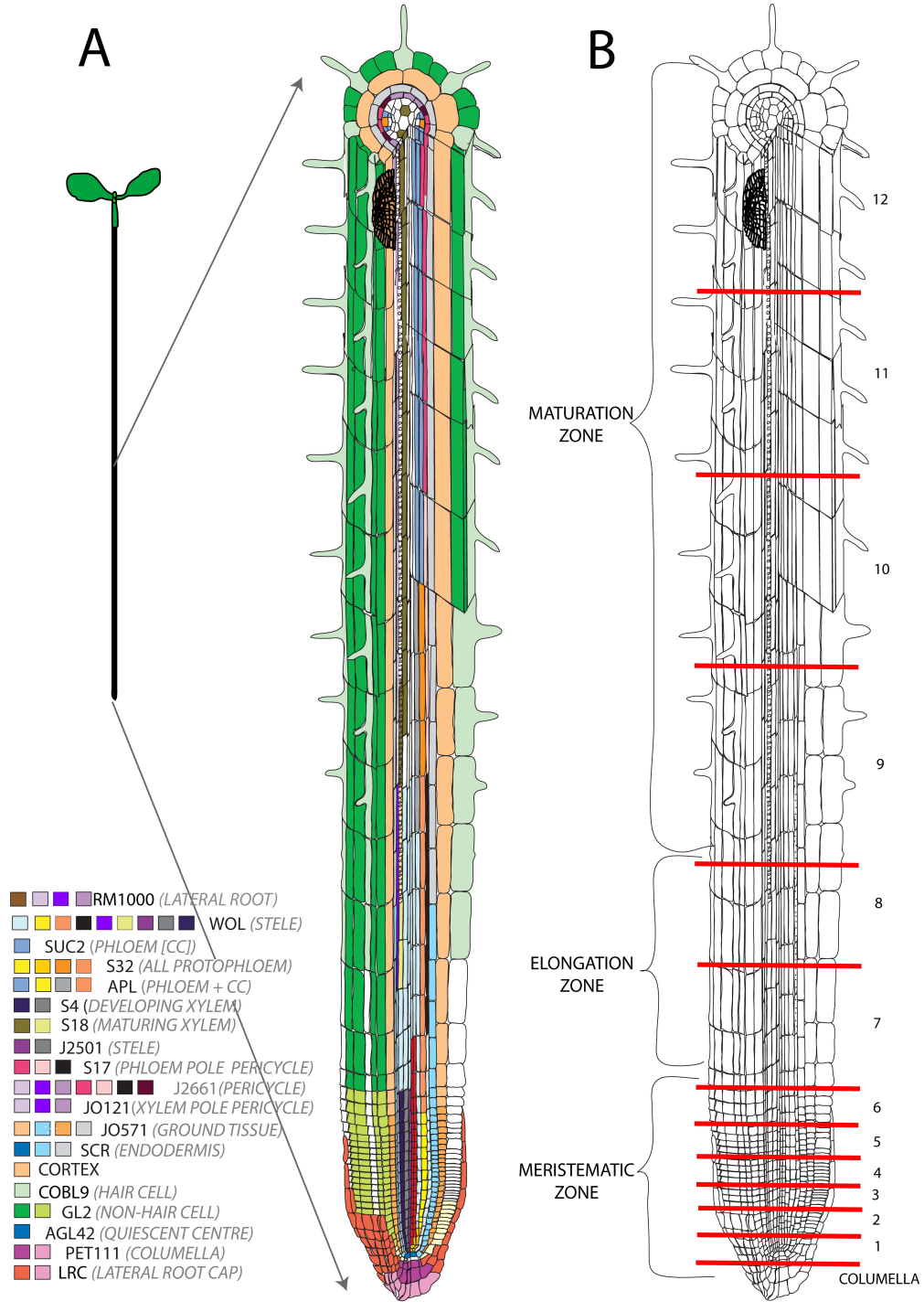
- Chemically, using 18 markers (colors in diagram A)
- Physically, using 13 longitudinal sections (red lines in diagram B)



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Naïve approach would use variation among each set of experiments as proxies for variation along each of the two axes.

Problem with naïve approach

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For example, the sample labelled APL consists of mixture of two cell types:

	cell type	
section	phloem	phloem companion cells
12	$\frac{1}{16}$	$\frac{1}{16}$
⋮	⋮	⋮
7	$\frac{1}{16}$	$\frac{1}{16}$
6	$\frac{1}{16}$	0
⋮	⋮	⋮
3	$\frac{1}{16}$	0
2	0	0
1	0	0
columella	0	0

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- In sections 6-12, there are no lateral root cap cells.

Conclusion: Need to analyze each transcript across all 31 $(= 13 + 18)$ experiments to model the expression pattern in the whole root.

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Under-constrained system: 31 $(= 13 + 18)$ functionals and 129 clusters.

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Example

If the expression level is either 0 or 1 (off or on), then our assumption says that it is 1 for the combination of some subset of the sections and some subset of the cell types.

Non-negative bilinear equations

$A^{(1)}, \ldots, A^{(k)}$ $n \times m$ non-negative matrices (cell mixture)

$o_1, \ldots, o_k$ non-negative scalars (expression levels)

Solve (approximately)

$$f_1(x, y) := x^t A^{(1)} y = o_1$$

$$\vdots$$

$$f_k(x, y) := x^t A^{(k)} y = o_k$$

$$x_1 + \cdots + x_n = 1$$

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for x and y non-negative vectors of dimensions $n \times 1$ and $m \times 1$ respectively.

Probabilistic interpretation

$$f_\ell(x, y) := \sum_{i,j} A_{ij}^{(\ell)} x_i y_j \text{ for } \ell = 1, \ldots, k$$

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1. Pick a pair of integers from $\{1, \ldots, n\} \times \{1, \ldots, m\}$ with (i, j) having probability proportional to

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2. Output an integer from $\{1,\ldots,k\}$. Conditional on having picked i and j in the previous step, the probability of outputing ℓ is:
$$A_{ij}^{(\ell)} / \left(\sum_\ell A_{ij}^{(\ell)}\right)$$

Maximum Likelihood Estimation

Rescaling both sides of our system of equations:

$$\frac{f_\ell(x,y)}{\sum_{\ell'} f_{\ell'}(x,y)} = \frac{o_\ell}{\sum_{\ell'} o_{\ell'}} \text{ for } \ell = 1,\ldots,k$$

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Finding an approximate solution to these equations is known as Maximum Likelihood Estimation.

Kullback-Leibler divergence

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We generalize divergence to any pair of non-negative vectors.
By approximate solution to a system, we will mean the a solution which minimizes the Kullback-Leibler divergence.

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- Estimate contribution of (i, j) term of left side of equation 1 needed to obtain equality:

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- Repeat until convergence

Likelihood maximization for monomial models

$$g : \mathbb{R}^n \times \mathbb{R}^m \to \mathbb{R}^{nm}$$
$$(x_i), (y_j) \mapsto A_{ij} x_i y_j$$

where $A_{ij} = \sum_\ell A_{ij}^{(\ell)}$.

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Moment map (taking row sums and column sums):

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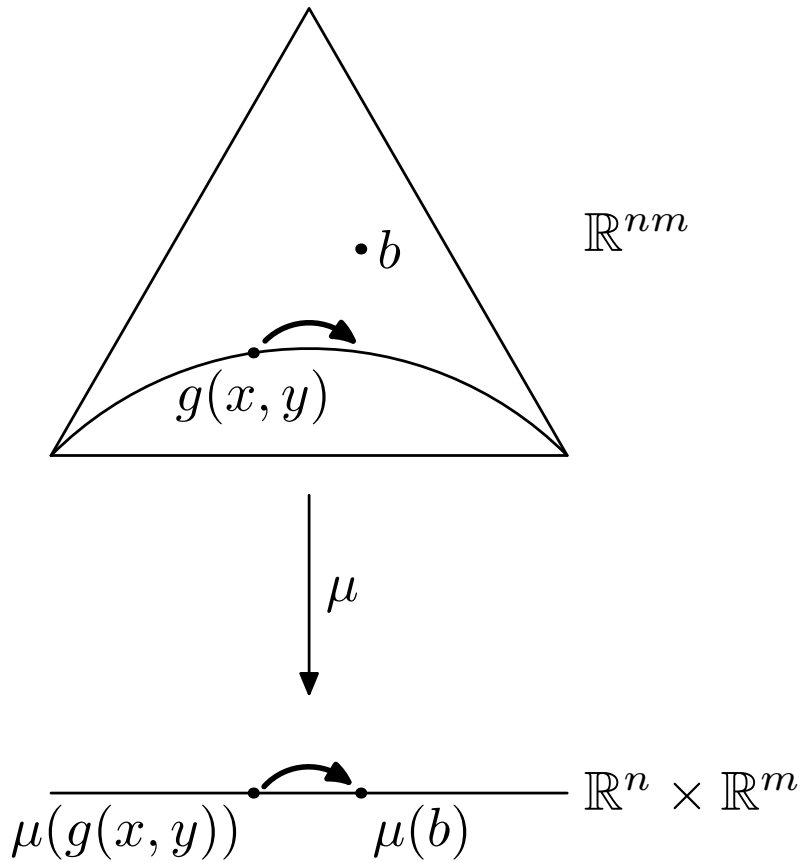
Theorem
Kullback-Leibler divergence $D(z\|g(x,y))$ is minimized over all x and y when $\mu(z)$ equals $\mu(g(x,y))$.

Inverting the moment map: Iterative Proportional Fitting



Inverting the moment map: Iterative Proportional Fitting

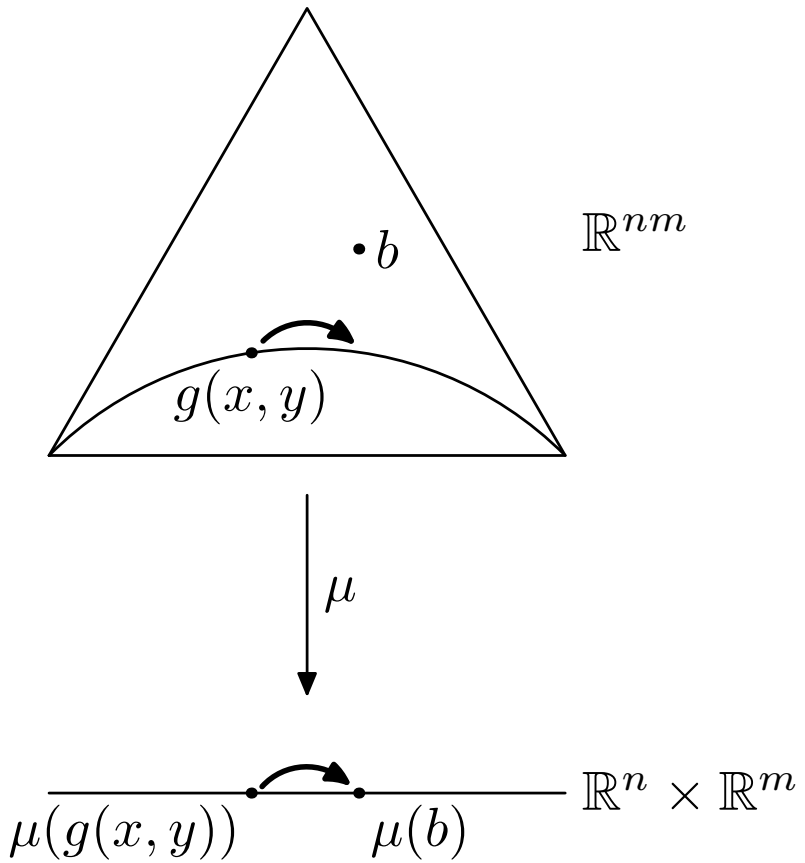
- Adjust $\tilde{x}_i$:

$$\tilde{x}_i \leftarrow \tilde{x}_i \frac{\sum_j b_{ij}}{\sum_j a_{ij} \tilde{x}_i \tilde{y}_j}$$

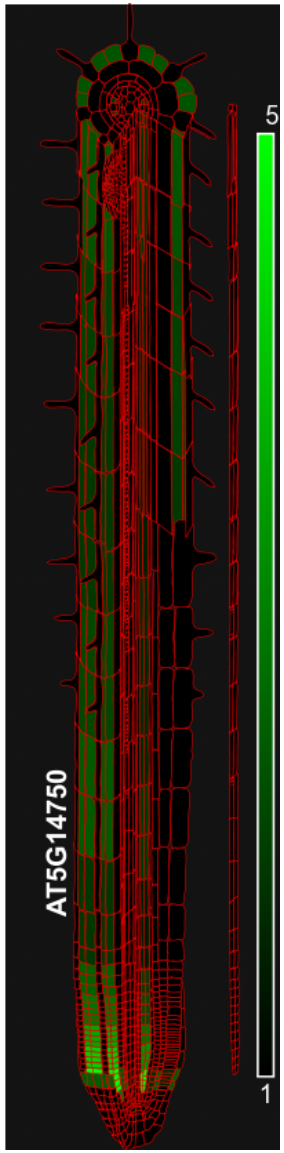
- Adjust $\tilde{y}_i$:

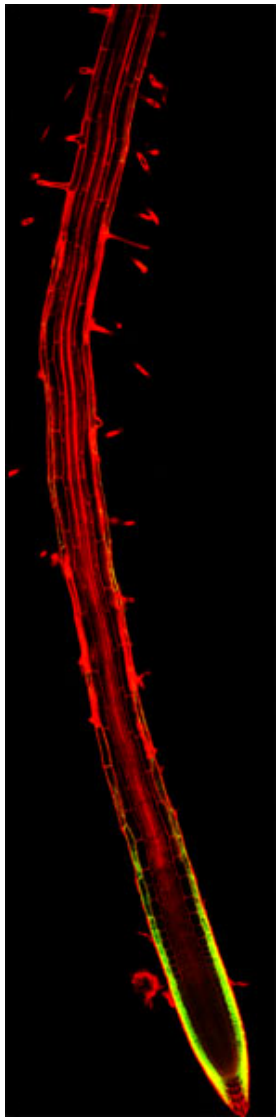
$$\tilde{y}_j \leftarrow \tilde{y}_j \frac{\sum_i b_{ij}}{\sum_i a_{ij} \tilde{x}_i \tilde{y}_j}$$

- Iterate until convergence



Validation: Preliminary results





On the left is a visual representation of the reconstructed expression levels.
On the right, the expression levels for the same transcript are visualized using GFP.