AgBioData
Coordinated Innovation Networks Grant

Title: AgBioData: A Coordinated, Collaborative and Innovative Network of Genomic, Genetic and Breeding Databases for Enhanced Agricultural Research Outcomes

USDA
National Institute of Food and Agriculture (NIFA)
Food and Agriculture Cyberinformatics and Tools Initiative (FACT)
https://nifa.usda.gov/program/fact

FACT focuses on data science to enable systems and communities to effectively utilize data, improve resource management, and integrate new technologies and approaches to further U.S. food and agriculture enterprises.

WHAT IS A COORDINATED INNOVATION NETWORK? Coordinated innovation networks projects foster communities that address critical areas by bringing together experts from different disciplines to identify solutions.

Letter of Intent submitted July 25, 2018. Accepted August 15, 2018

Dorrie Main is Project Director. If funded funds will go to:

- Wash State for yearly workshop, and website support (10% FTE)
- Iowa State University for 50% FTE coordinator (J Campbell)
- Phoenix Bioinformatics for Database Sustainability Pilot Study

Objectives:

1: Develop and implement standards for AgBioData data curation

2: Establish common practices for broad use of ontologies, specifically GO, PO, TO and PATO, and provide tools and training for researchers

3: Establish metadata standards across AgBioData members and promote compliance

4: Identify opportunities for a federated model of data exchange for AgBioData member databases.

5: Identify funding options for long term database sustainability

6: Work with funding agencies and journals to enhance data provision by researchers

Timeline:

1. Sept 15: Steering Committee Draft to Whole group
2. Oct 19: Submitted to WSU Grants Office

So, please plan to help in the area most near to your interests between Sept 15 and October 19. THANKS!!!!

We would like to include a representative from each database/resource as an official collaborator on the proposal – will be in touch soon to request letter if this is agreeable

Note about the Steering Committee:
We are slowly thinking about governance bylaws for AgBioData. We WILL rotate people onto the Steering committee (maybe by election), and we hope to start this process as soon as the grant is in.

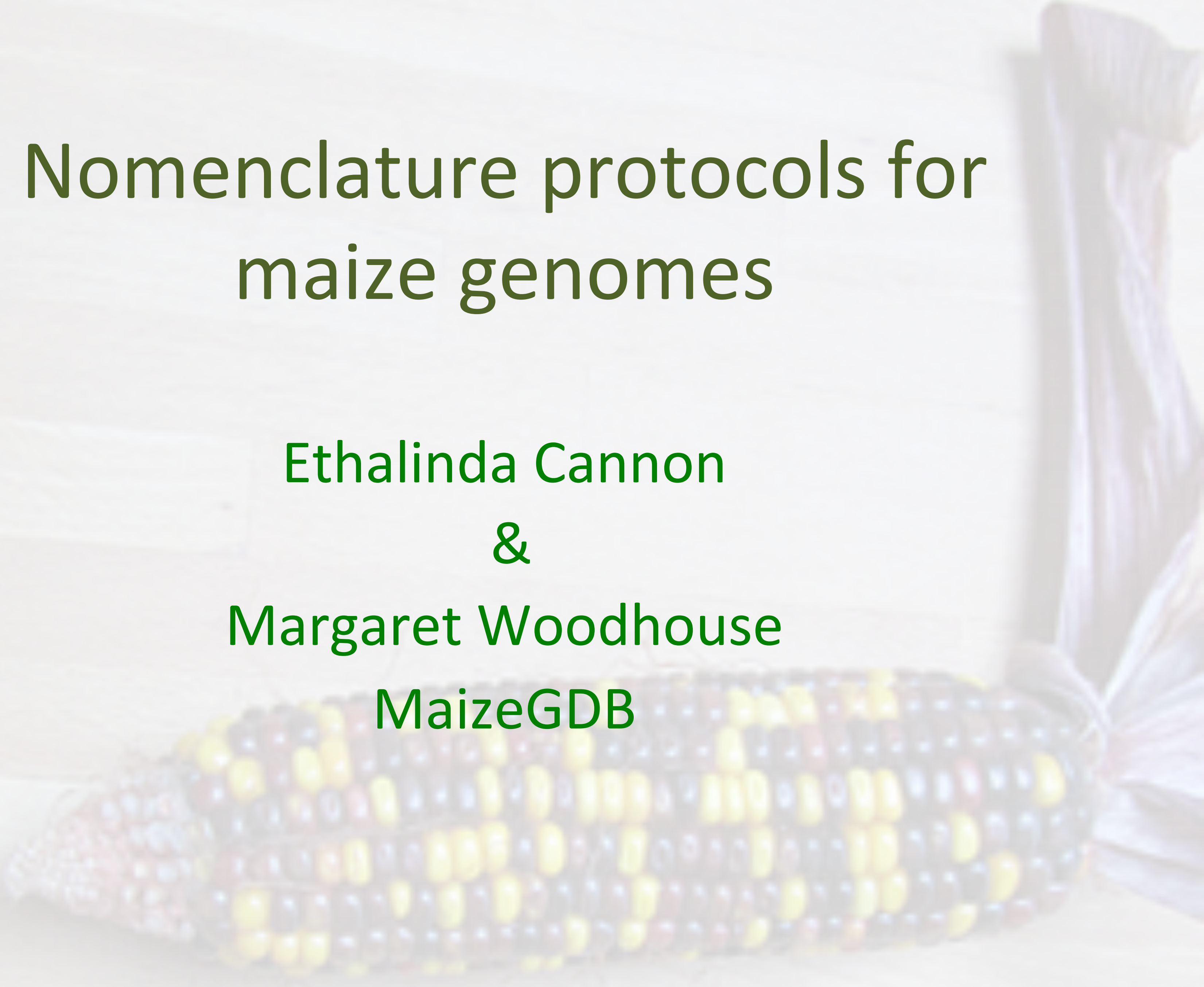
TODAYS MEETING:

Genome Nomenclature in various organisms

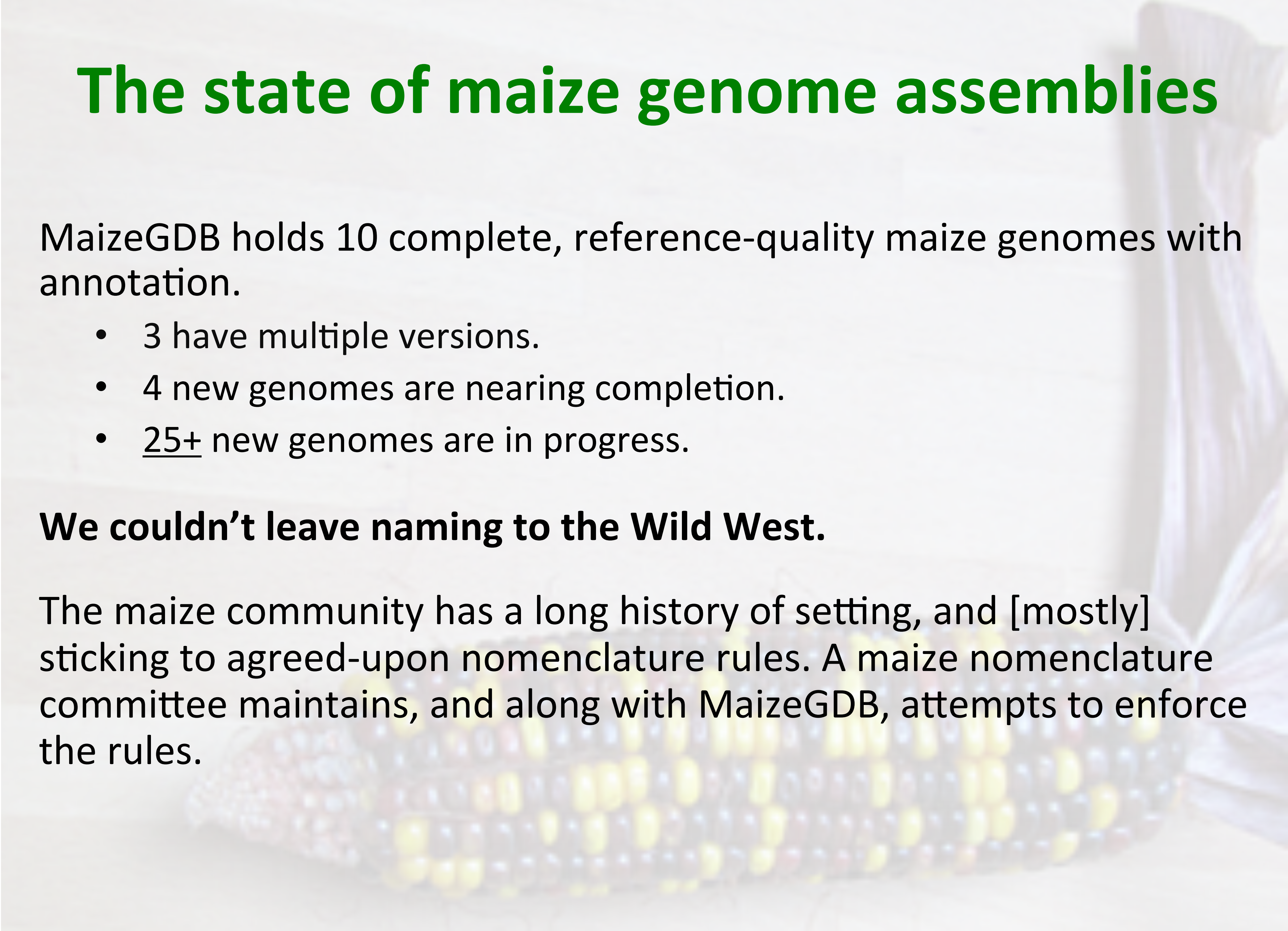
Ethy/Maggie: Maize
Tanya: Arabidopsis
Sook: Prunus, Cotton
Marcela: Many- Ensemble
Pankaj: Many- Planteome
Taner: Wheat

Nomenclature protocols for maize genomes

Ethalinda Cannon
&
Margaret Woodhouse
MaizeGDB



The state of maize genome assemblies



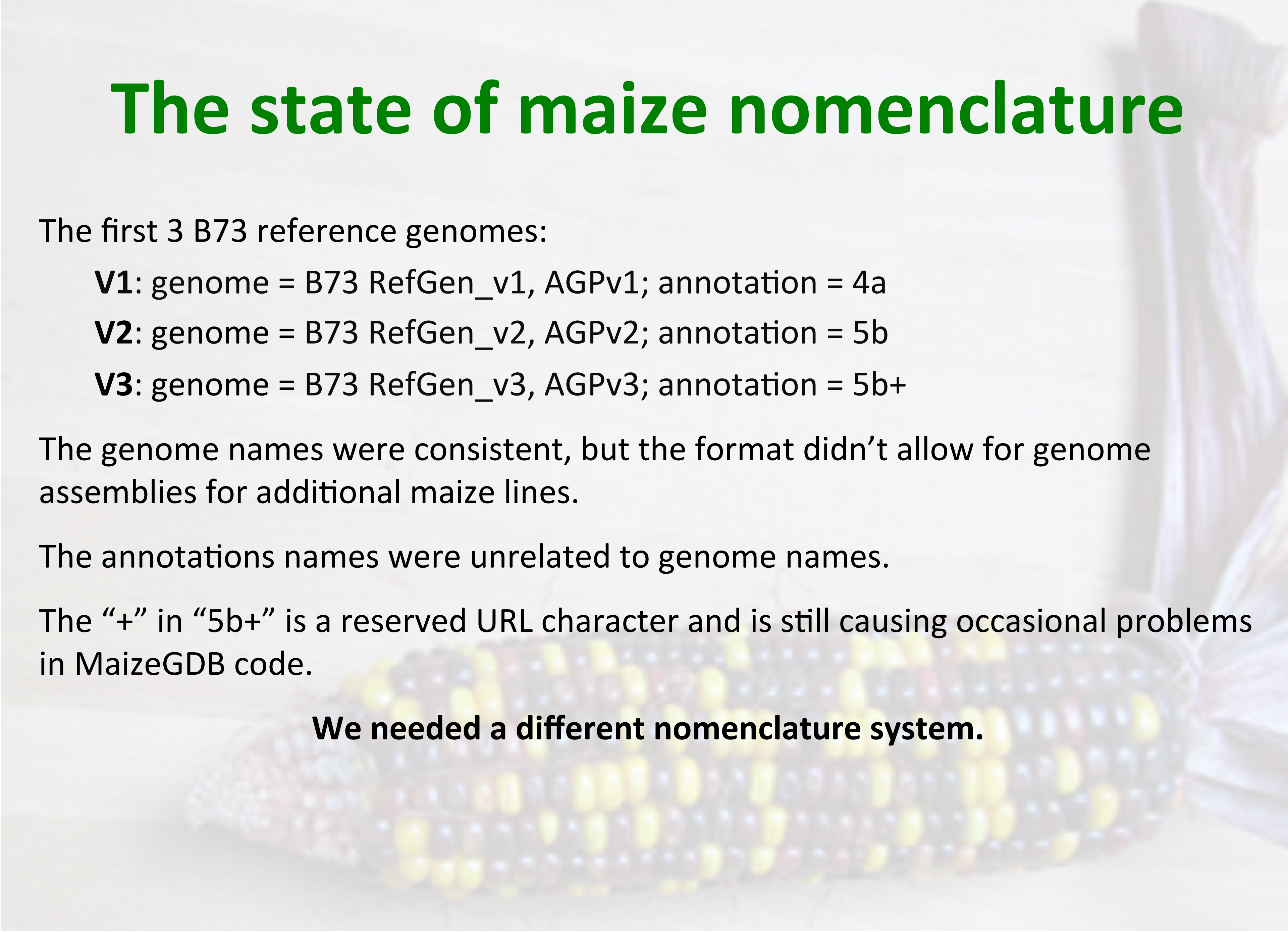
MaizeGDB holds 10 complete, reference-quality maize genomes with annotation.

- 3 have multiple versions.
- 4 new genomes are nearing completion.
- 25+ new genomes are in progress.

We couldn't leave naming to the Wild West.

The maize community has a long history of setting, and [mostly] sticking to agreed-upon nomenclature rules. A maize nomenclature committee maintains, and along with MaizeGDB, attempts to enforce the rules.

The state of maize nomenclature



The first 3 B73 reference genomes:

- **V1**: genome = B73 RefGen_v1, AGPv1; annotation = 4a
- **V2**: genome = B73 RefGen_v2, AGPv2; annotation = 5b
- **V3**: genome = B73 RefGen_v3, AGPv3; annotation = 5b+

The genome names were consistent, but the format didn't allow for genome assemblies for additional maize lines.

The annotations names were unrelated to genome names.

The "+" in "5b+" is a reserved URL character and is still causing occasional problems in MaizeGDB code.

We needed a different nomenclature system.

1. Naming maize genome assemblies

Objectives:

- Unique
- Consistent
- Human- and machine-readable
- Short
- Enforced across the maize research community
- No reserved symbols

This task was surprisingly difficult.

1. Naming maize genome assemblies

Assembly identifiers: (Caution when encoding information in identifiers)

Z(species)-(cultivar or accession)-(DRAFT/REFERENCE)-(group)-(version)

For instance, B73 version 4 is officially named:

Zm-B73-REFERENCE-GRAMENE-4.0

Zm: *Zea mays.*

B73: The cultivar.

REFERENCE: This is the reference genome for B73 ("reference" means a pseudomolecule assembly as opposed to unassembled scaffolds, which are denoted "DRAFT").

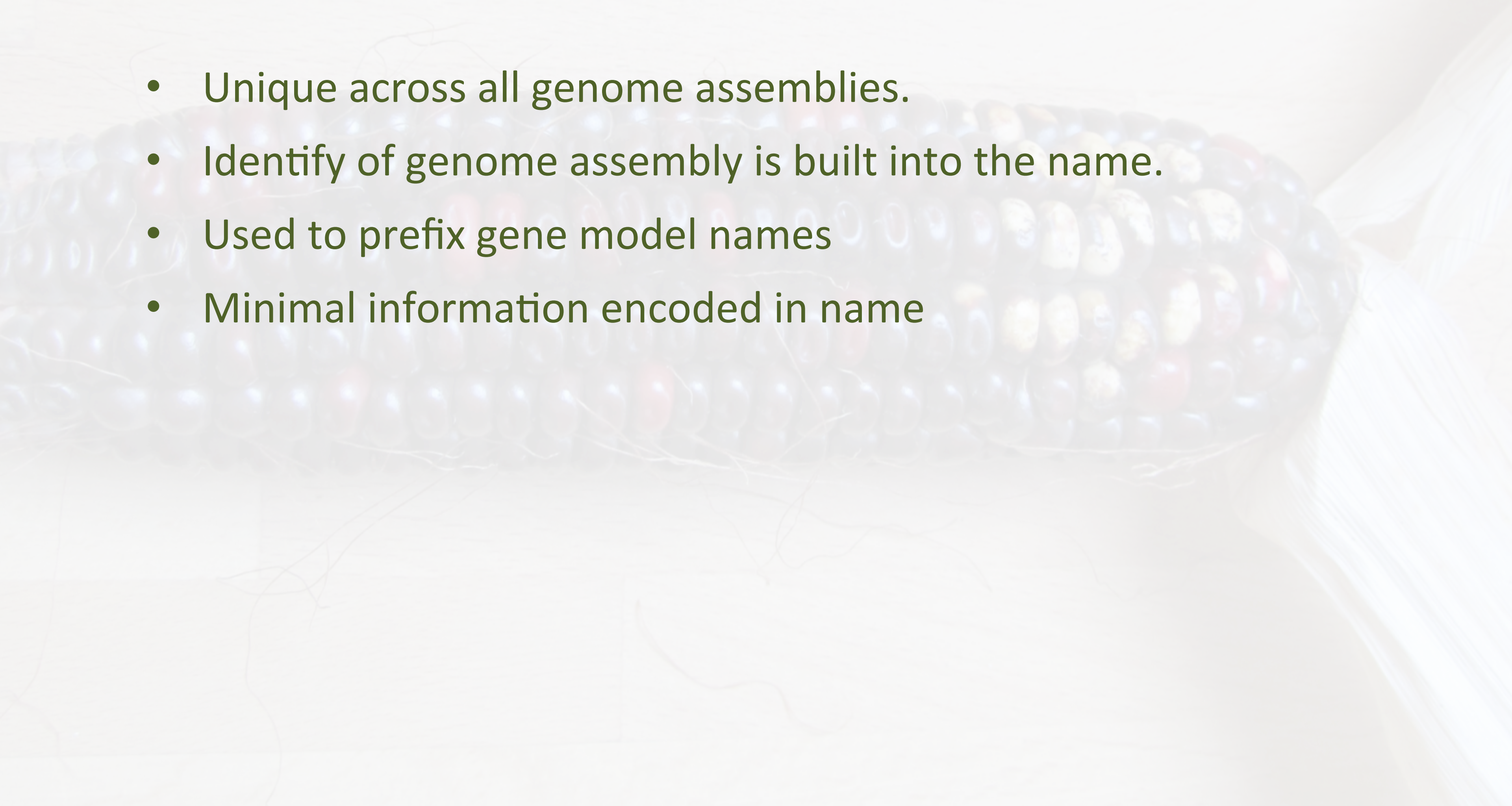
GRAMENE: the group that sequenced version 4.

4.0: This is the fourth version of the B73 genome

2. Naming maize genome annotations

Annotations have a shorter name.

- Unique across all genome assemblies.
- Identify of genome assembly is built into the name.
- Used to prefix gene model names
- Minimal information encoded in name



2. Naming maize genome annotations

Annotation identifiers:

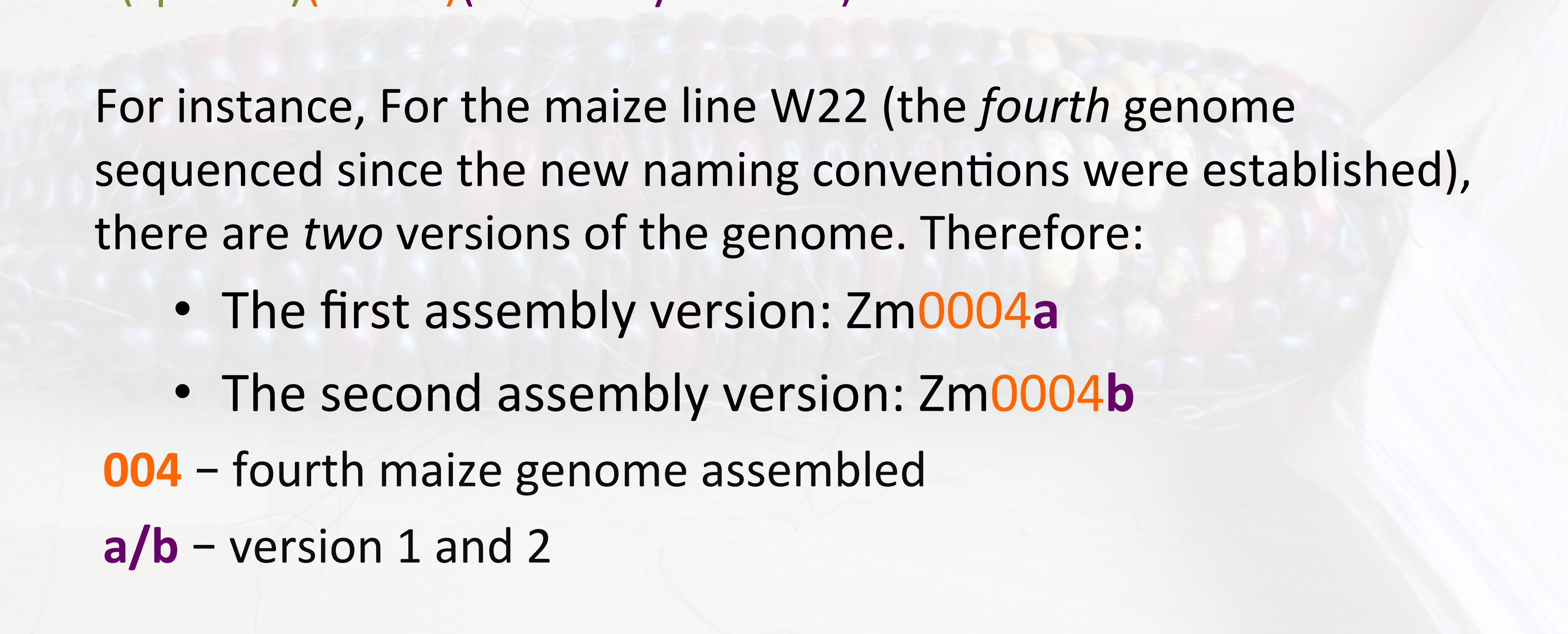
Z(species)(series)(assembly version)

For instance, For the maize line W22 (the *fourth* genome sequenced since the new naming conventions were established), there are *two* versions of the genome. Therefore:

- The first assembly version: Zm0004**a**
- The second assembly version: Zm0004**b**

004 – fourth maize genome assembled

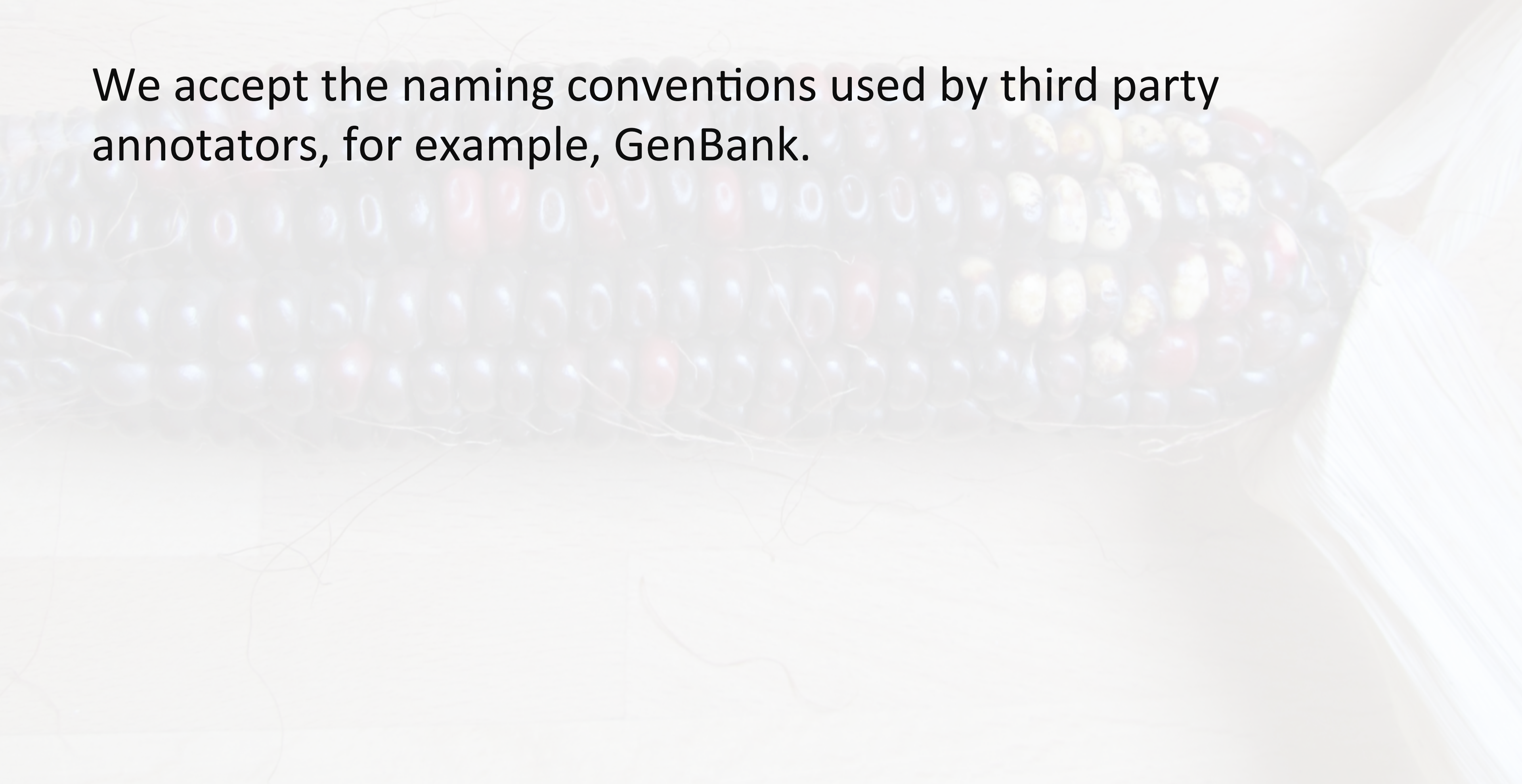
a/b – version 1 and 2



2. Naming maize genome annotations

Third party annotations

We accept the naming conventions used by third party annotators, for example, GenBank.



3. Naming maize gene models

Objectives:

- Short names.
- Assembly built into name.
- Unique across all genome assemblies.
- Applies only to the “reference” annotation (others use their own conventions, e.g. NCBI).
- Numbering should not imply gene location or order*.

***this is controversial!**

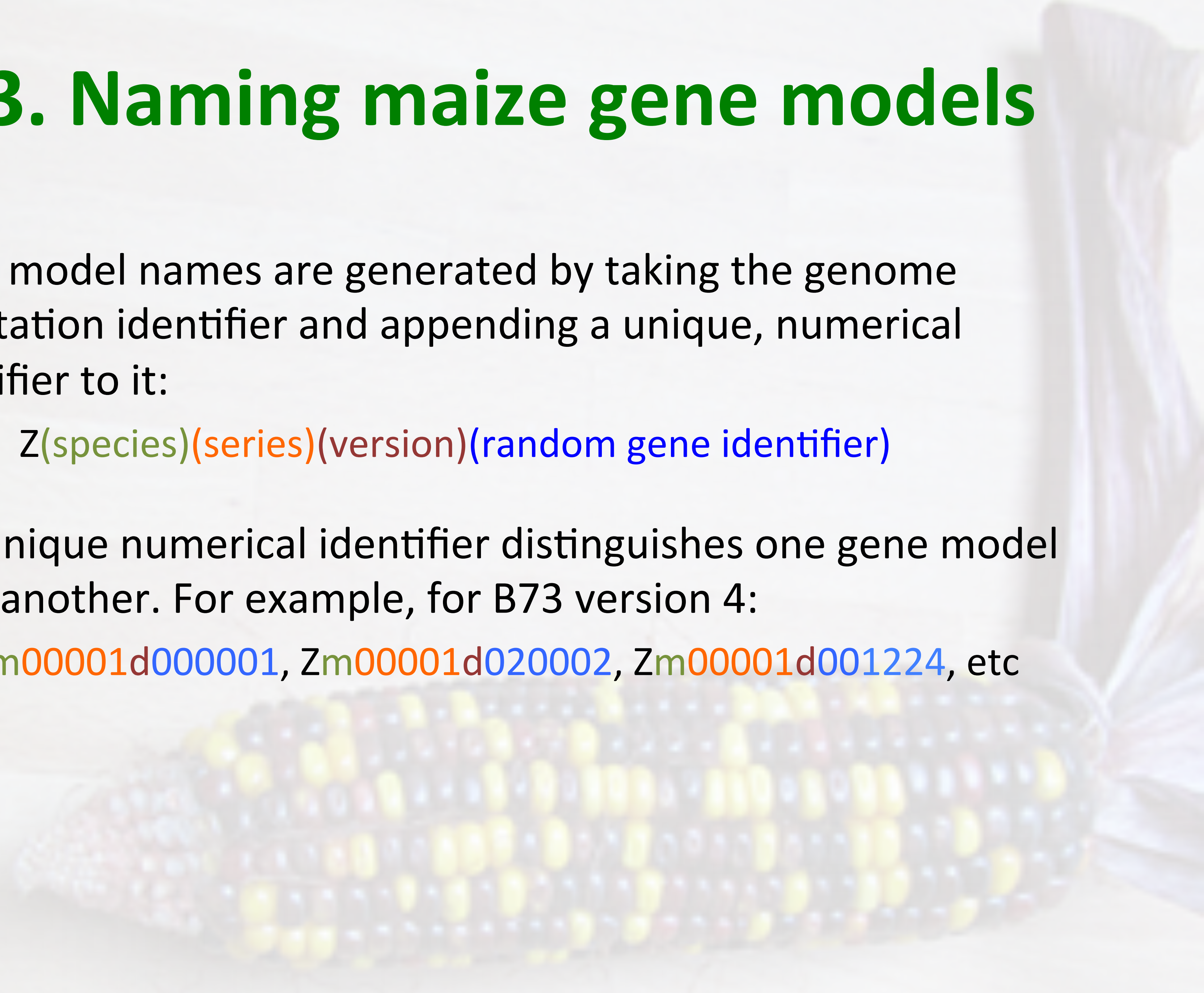
3. Naming maize gene models

Gene model names are generated by taking the genome annotation identifier and appending a unique, numerical identifier to it:

Z(species)(series)(version)(random gene identifier)

The unique numerical identifier distinguishes one gene model from another. For example, for B73 version 4:

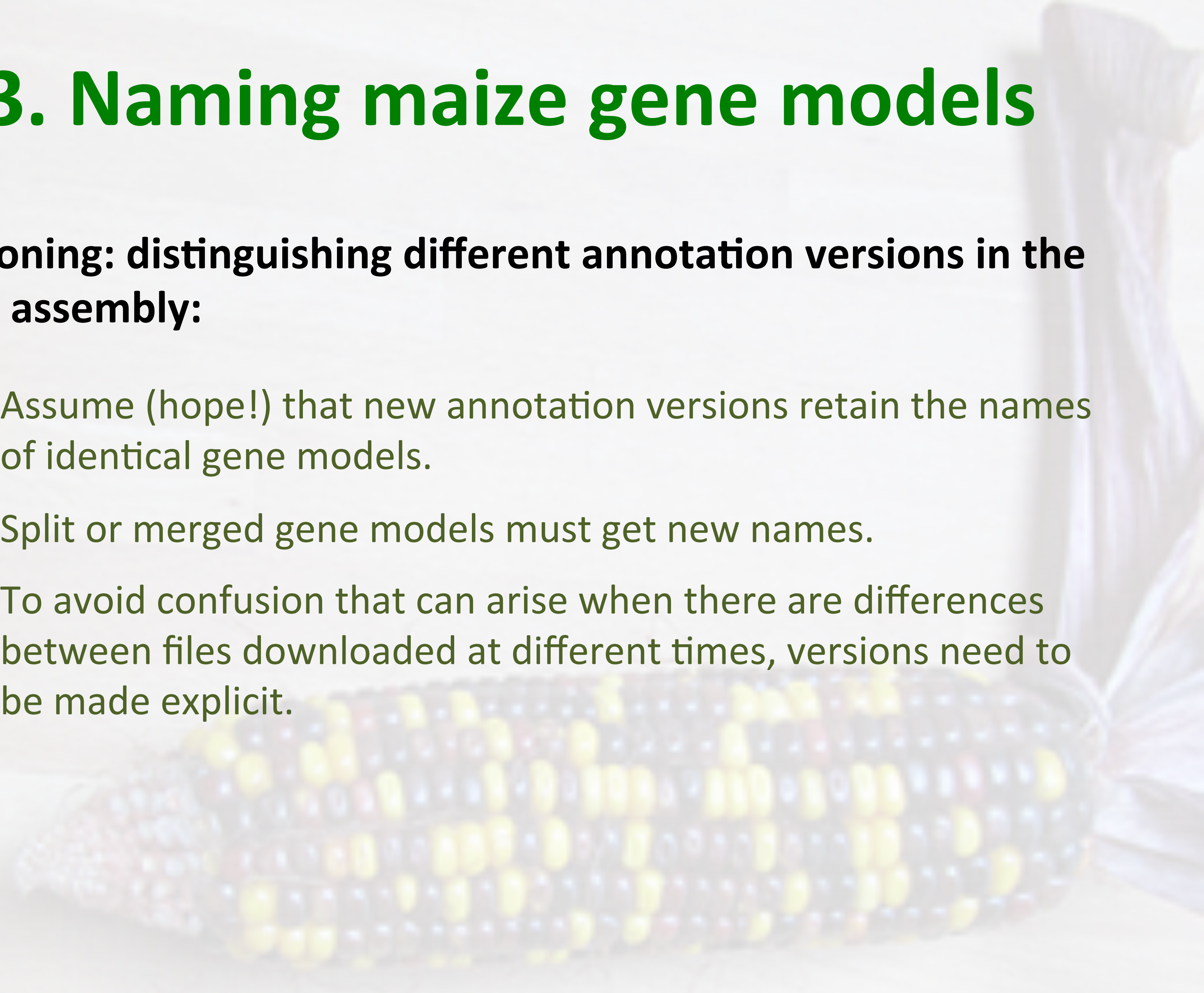
Zm00001d000001, Zm00001d020002, Zm00001d001224, etc



3. Naming maize gene models

Versioning: distinguishing different annotation versions in the <u>same</u> assembly:

- Assume (hope!) that new annotation versions retain the names of identical gene models.
- Split or merged gene models must get new names.
- To avoid confusion that can arise when there are differences between files downloaded at different times, versions need to be made explicit.



3. Naming maize gene models

Versioning: distinguishing different annotation versions in the same assembly:

Z(species)(series)(assembly version).(annotation version)

For example, the current annotation for B73 v4 is:

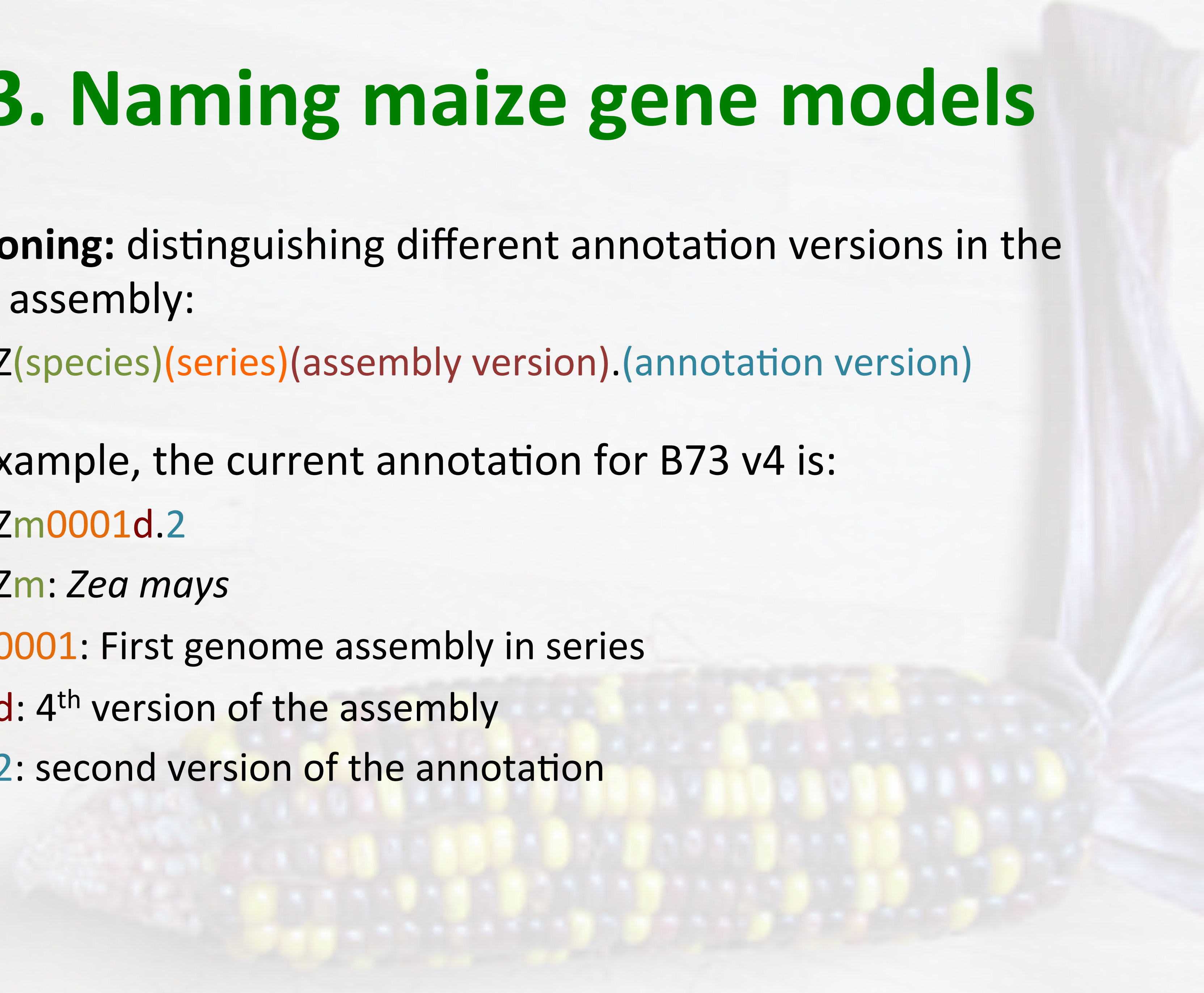
Zm0001d.2

Zm: *Zea mays*

0001: First genome assembly in series

d: 4th version of the assembly

2: second version of the annotation

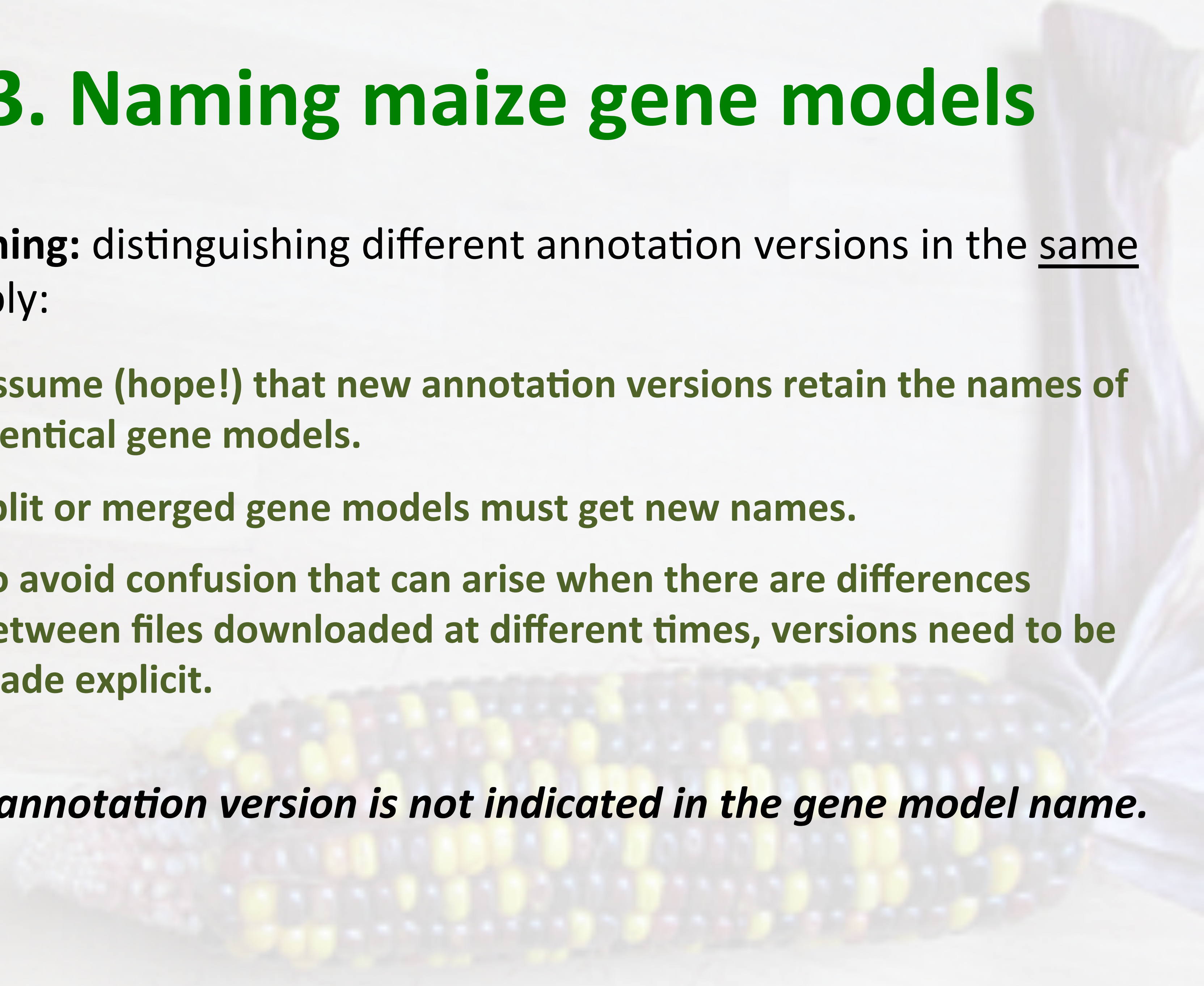


3. Naming maize gene models

Versioning: distinguishing different annotation versions in the same assembly:

- **Assume (hope!) that new annotation versions retain the names of identical gene models.**
- **Split or merged gene models must get new names.**
- **To avoid confusion that can arise when there are differences between files downloaded at different times, versions need to be made explicit.**

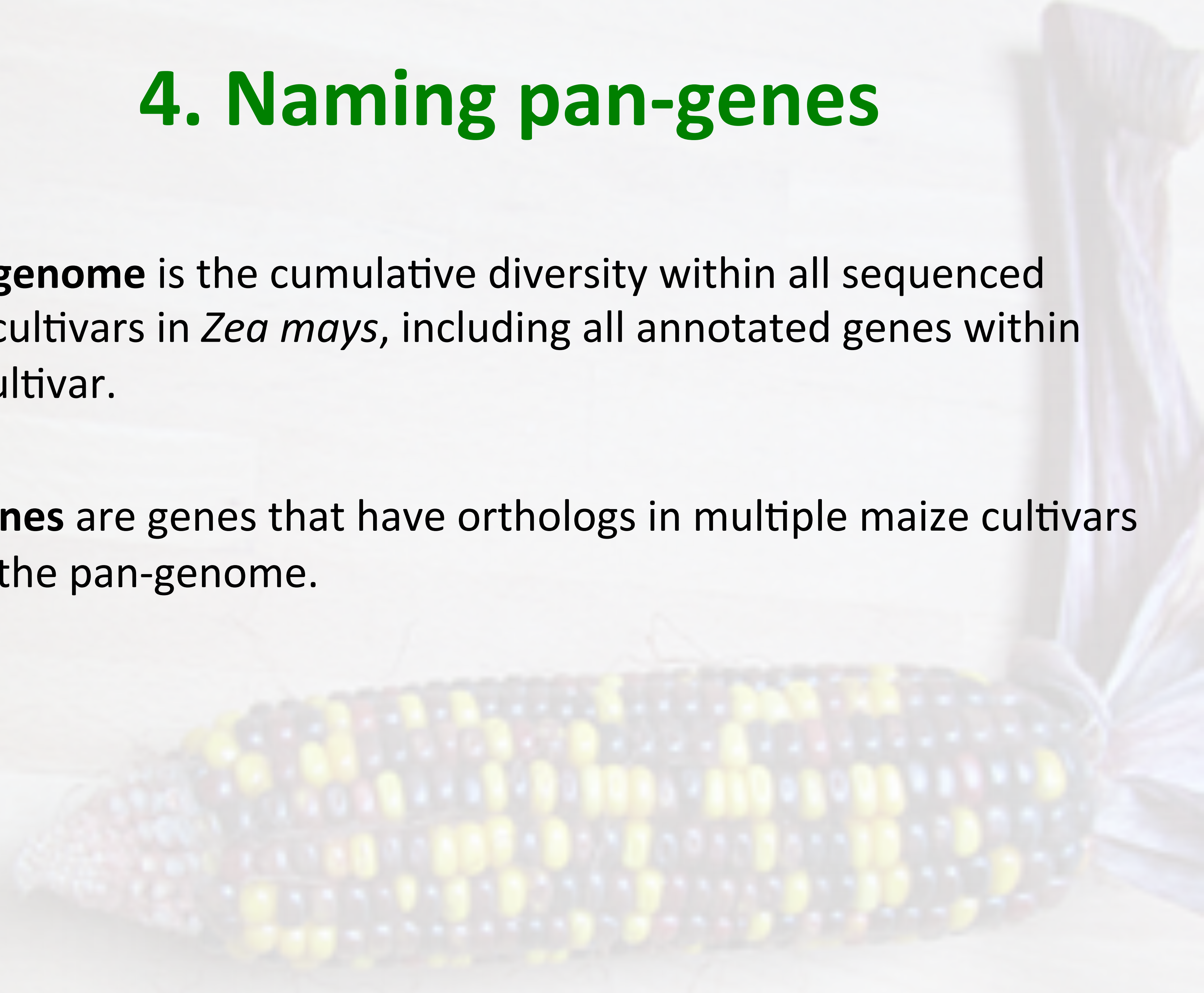
The annotation version is not indicated in the gene model name.



4. Naming pan-genes

A **pan-genome** is the cumulative diversity within all sequenced maize cultivars in *Zea mays*, including all annotated genes within each cultivar.

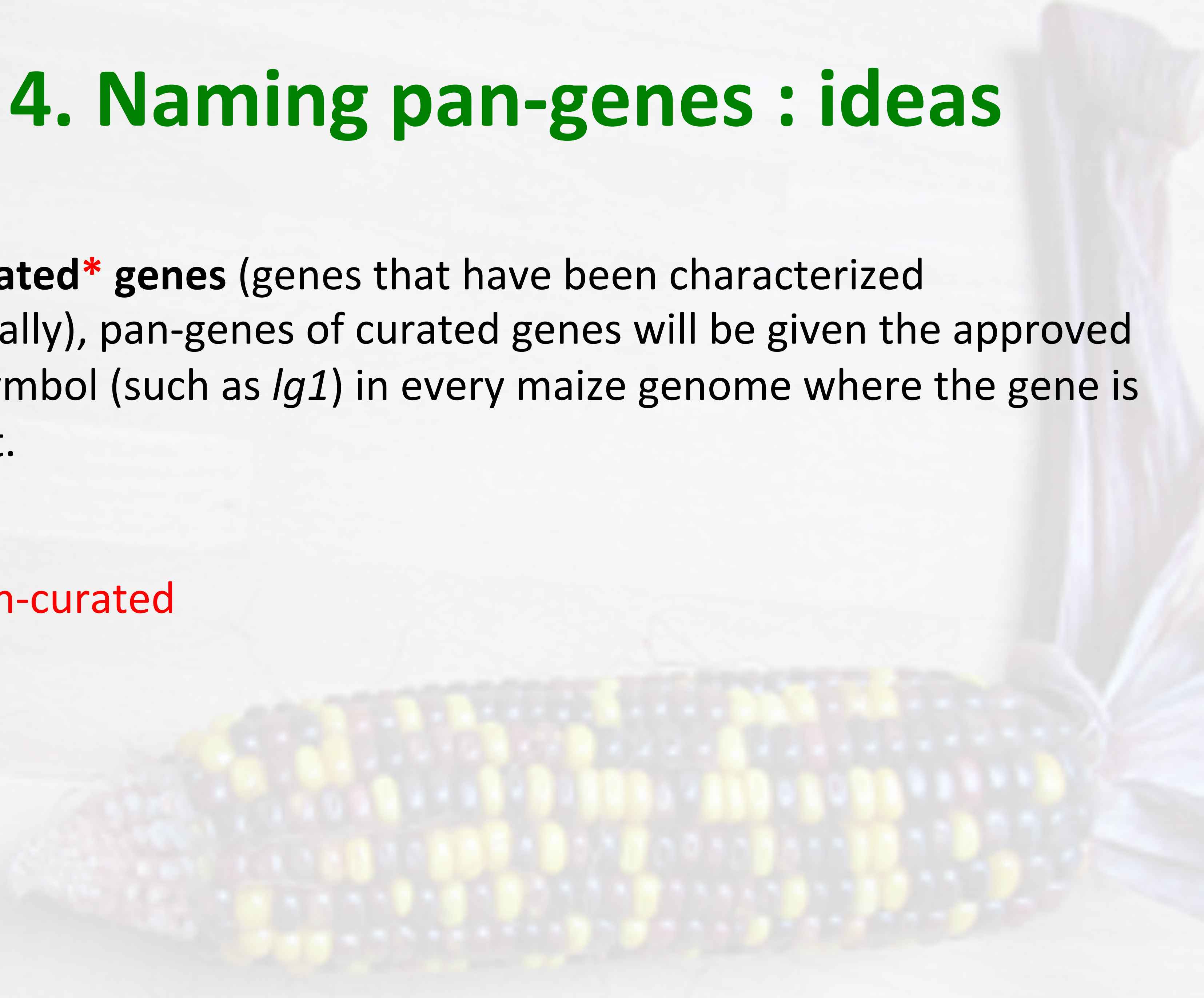
Pan-genes are genes that have orthologs in multiple maize cultivars within the pan-genome.



4. Naming pan-genes : ideas

For **curated*** **genes** (genes that have been characterized genetically), pan-genes of curated genes will be given the approved gene symbol (such as *lg1*) in every maize genome where the gene is present.

*human-curated

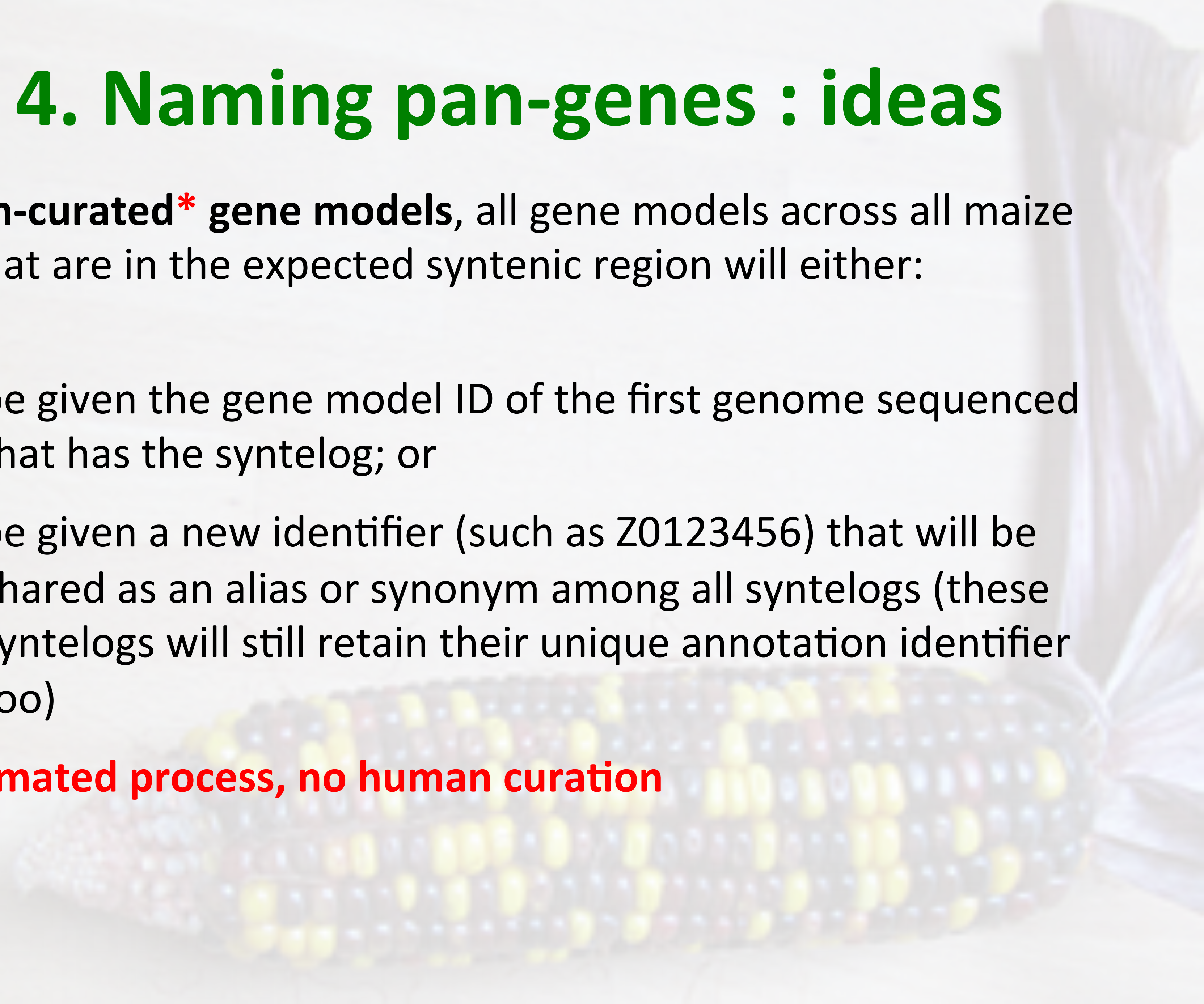


4. Naming pan-genes : ideas

For **non-curated* gene models**, all gene models across all maize lines that are in the expected syntenic region will either:

- be given the gene model ID of the first genome sequenced that has the syntelog; or
- be given a new identifier (such as Z0123456) that will be shared as an alias or synonym among all syntelogs (these syntelogs will still retain their unique annotation identifier too)

*** Automated process, no human curation**



Arabidopsis thaliana genome annotation

The story so far

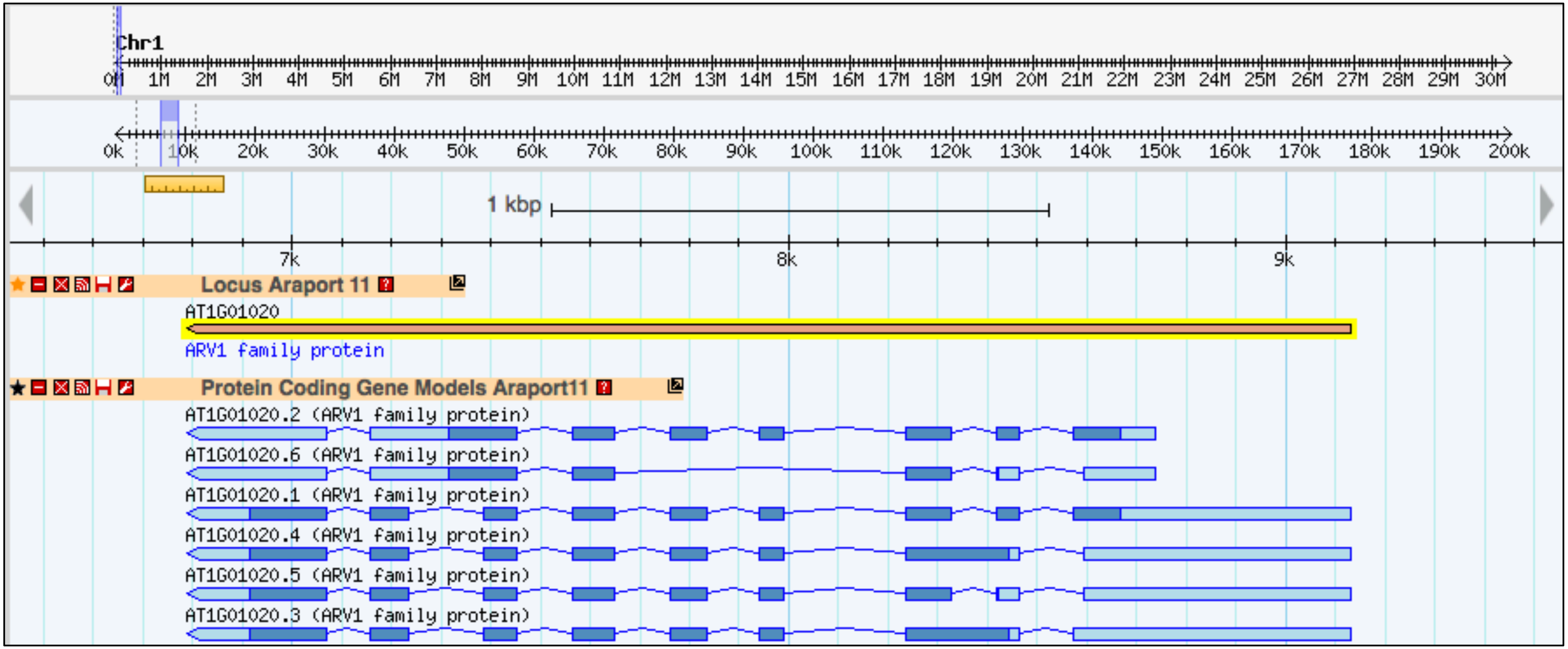
History of *A. thaliana* genome annotation

- Original annotation:
  - 2000: Completion of genome sequence, TIGR1 genome release
- Reannotation (10 versions)
  - 2005: TAIR6 genome release
  - 2016: Araport11 genome release
- 20??: Next genome release

Source Germplasm = Col-0

- **Past:** Multiple Col-0 stocks used, unclear how these were related to each other.
- **Proposal:** Col-0 seed stock CS70000 designated as the reference seed stock.

Naming Conventions


Chr1
0M 1M 2M 3M 4M 5M 6M 7M 8M 9M 10M 11M 12M 13M 14M 15M 16M 17M 18M 19M 20M 21M 22M 23M 24M 25M 26M 27M 28M 29M 30M
0k 10k 20k 30k 40k 50k 60k 70k 80k 90k 100k 110k 120k 130k 140k 150k 160k 170k 180k 190k 200k
1 kbp
7k
8k
9k
Locus Araport 11
AT1G01020
ARV1 family protein
Protein Coding Gene Models Araport11
AT1G01020.2 (ARV1 family protein)
AT1G01020.6 (ARV1 family protein)
AT1G01020.1 (ARV1 family protein)
AT1G01020.4 (ARV1 family protein)
AT1G01020.5 (ARV1 family protein)
AT1G01020.3 (ARV1 family protein)

- **AT[1-5,C,M)gNNNNN**
- **Locus:** At1g01020
- **Gene model:** At1g01020.1, At1g01020.2, …

- Currently no distinction in naming between genome assembly (pseudo-chromosomes) and gene annotation (individual gene calls)
  - – TAIR10 genome assembly (same as TAIR9)
  - – TAIR10 gene annotation (different from TAIR9)
- Not ideal approach – need to be able to version/name them independently

Existing/Upcoming issues

- L*er* sequence published– used AGI identifier approach but inconsistent use between Col-0 and Ler use
  - Col-0 At1g01040 != L*er* At1g01040
  - Created mapping file with author-supplied source files
- ‘Platinum’ standard, PacBio sequences (de novo assembly) of Col-0, L*er*, up to 50 other ecotypes coming – need for a consistent nomenclature approach
- Many other ecotypes are sequenced with Col-0 reference guided assembly (1001 genomes project) and could/should be annotated
- Variation in gene insertion/deletion/rearrangement/ modification in other ecotypes vs. Col-0

Handling user feedback

- Accumulate suggestions between releases
  - Need for tracking, verification, standards for acceptance of edits
- Incremental updates? How to propagate these efficiently and effectively – NCBI/DDBJ/EMBL and others

GENOME NAMING GUIDELINE IN GDR
(AND COTTONGEN, CGD, CSFL)

Sook Jung
Washington State University

Genome Naming Guideline

- [Genus] [species] genome v[assembly version].a[annotation-version]
- Example: **Prunus persica genome v2.0.a1**
- Where:
  - Genus = the genus of the organism
  - Species = the species of the organism
  - Assembly version = the version of the assembly with a major and minor number. The major version is incremented with major changes or releases of the assembly and the minor number is incremented when minor changes are made to the assembly.
  - Annotation-version = a single numeric value that is incremented each time a new annotation is released. It restarts at 1 each time the assembly version is incremented.

It works most of the time
(GDR has 21 genome assemblies from 7 crops and 14 species)

- Prunus persica Genome v2.0.a1
- Prunus persica Genome v1.0
- Prunus avium Genome v1.0.a1
- Pyrus communis Genome v1.0

Multiple genome assemblies from the same species – add accession name

- Malus x domestica Genome v1.0.a1
- Malus x domestica Genome v2.0.a1
- Malus x domestica Genome v3.0.a1
- Malus x domestica GDDH13 Whole Genome v1.1
  - Up to v3.0 was done using heterozygous Golden Delicious, and the newest version was done using GDDH13, a doubled-haploid Golden Delicious tree.

Multiple genome assembly with the same accession? – add institution name.

- CottonGEN example
  - Gossypium hirsutum (AD1) acc 'TM-1' genome CGP-BGI v1.1 assembly & v1.0 annotation
  - Gossypium hirsutum (AD1) acc 'TM-1' genome NAU-NBI v1.1 assembly & v1.1 annotation
  - Gossypium hirsutum (AD1) acc 'TM-1' genome UTX-JGI v1.0 assembly v1.0

- **Same accession and institution?** Use published name.
  - Rosa chinensis Genome v1.0
  - Rosa chinensis Old Blush homozygous Genome v2.0
    - Rosa chinensis Old Blush Illumina genome v1.0

Sometimes authors skip versions when they publish..

- Fragaria vesca Genome v1.0.a1
- Fragaria vesca Genome v1.1.a1
- Fragaria vesca Genome v1.1.a2
- Fragaria vesca Genome v2.0.a1
- Fragaria vesca Genome v2.0.a2
- Fragaria vesca Genome v4.0.a1

Some times authors publish duplicated names

- Fragaria vesca Genome v1.0.a1
- Fragaria vesca Genome v1.1.a1
- Fragaria vesca Genome v1.1.a2
- Fragaria vesca Genome v2.0.a1
  - Fragaria vesca Genome v1.1.a2 (Darwish et al. 2014) track – we originally called it Fragaria vesca Genome v2.0.a2
- Fragaria vesca Genome v2.0.a2
  - Fragaria v2.0.a2 (Li et al. 2017)

conclusion

- Need to refine the naming system
- Need to work with journals and communities

Perspectives on genome nomenclature from 56 species

Marcela Karey Tello-Ruiz, PhD

September 5th, 2018

For AgBioData Consortium Nomenclature Discussion

Various Gene IDs systems @ Gramene/Ensembl Plants

- Reuse gene IDs assigned by the genome projects responsible for the annotation and provided to the INSDC:
    - NCBI: GenBank
    - EMBL-EBI: ENA
    - DDBJ: DDBJ
- Gramene/Plant Reactome/Ensembl Plants work with the INSDC (mainly ENA) to resolve IDs (prioritizing UniProt proteome-based IDs, if applicable).
- Adopt a system agreed/adopted by the community early on
- Provide a mechanism (ID converter) for mapping back to IDs in previous versions, when possible
- MODs and other resources work with GenBank/ENA to get a clear picture of how IDs are constructed

Species	Assembly	Gene Annotation	Gene ID example
Arabidopsis lyrata	Araly1.0	Araly1.0	Al_scaffold_0001_1000
Arabidopsis thaliana	TAIR10	AraPort11	AT3G52430
Chlamydomonas reinhardtii	v5.5 (GCA_000002595.3)	JGI via ENA	CHLRE_15g637761v5
Oryza sativa japonica	IRGSP-1.0	RAP-DB	Os05g0113900
Solanum lycopersicum	SL2.50	ITAG2.3	Solyc01g087250.2
Sorghum bicolor	V3 (GCA_000003195.3)	JGI via ENA	SORBI_3004G141800
Triticum aestivum	IWGSC v1.0	IWGSC v1.0	TraesCS3D01G273600
Vitis vinifera	IGGP 12x	2012-07-CRIBI	VIT_01s0010g03900
Zea mays	B73_RefGen_v4	MAKER-CSHL	Zm00001d048577

- In the near future, we will see the assemblies stabilizing, but the annotations updated based on evidence.
- Gene annotations: protein-coding, non-coding RNAs, pseudogenes.
- Regulatory features???

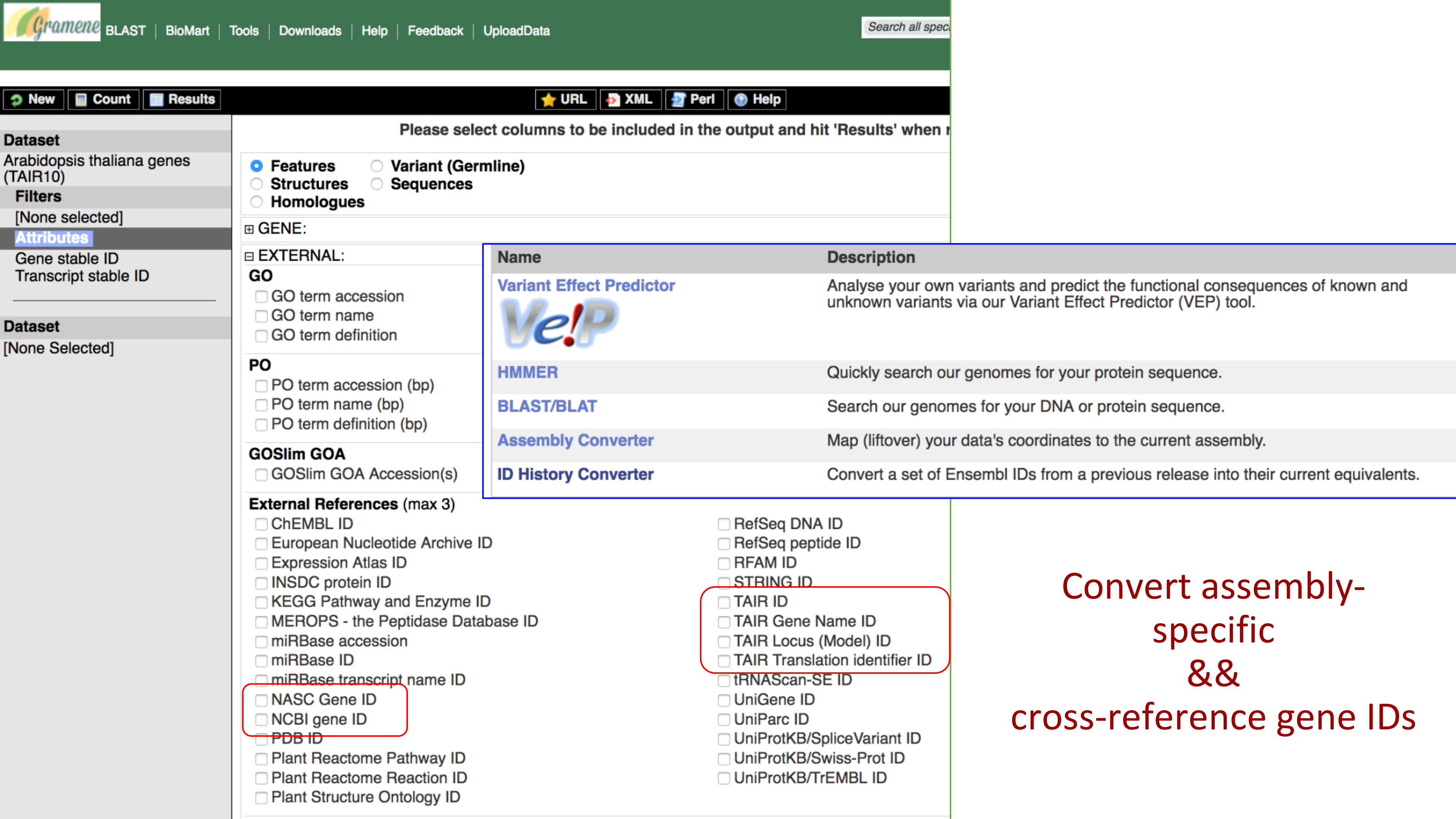
Full table in Gramene's release notes (56 species)
http://www.gramene.org/release-notes-58

Challenges

1. Lack of continuity in gene IDs/names
2. Caution on including too much information in a name
3. Propagating gene information between versions of the reference assembly. Many different approaches based on the quality of the draft assembly and the complexity of the organism.
4. Challenges associated with initial submission and updates to NCBI
5. Not all proteomes fully represented/updated @ UniProt
6. PanGenomes: Moving from a single reference to many references
    - Same as above but more complex
    - Learn from experience: *Arabidopsis thaliana* & *A. lyrata*
    - Grape: suggestion to include species and cultivar names (prefix/suffix letter codes) and numeric ID across species (some gene models will be species-specific).

Proposed naming strategy for the grape pangenome

- Annotate species and varieties in a gene ID.
  - *Species:* Community follows UniProt recommendation. First two letters of species name as prefix. Example: **Vitci** for *Vitis cisera* (ask UniProt to add species if not in the list: http://www.uniprot.org/docs/speclist).
  - *Cultivar:* Annotate the cultivar in the suffix (2-4 letters code), as they are basically considered different alleles. Examples: Use the prefix **Vitvi** (*V. vinifera*) for cabernet sauvignon (cs), pinot noir (pn), and flame, then suffix for cultivar (**Vitvi00g0000-cs** is a cab gene). Concord is a *V. labrusca* (**Vitla)**, add suffix.
- Relating orthologous genes. Compare the sequences to the latest release of a gene annotation for IDs to match. A challenging workflow that requires renaming and transformation of the IDs...


Gramene
BLAST | BioMart | Tools | Downloads | Help | Feedback | UploadData
Search all speci
New
Count
Results
URL
XML
Perl
Help

Please select columns to be included in the output and hit 'Results' when r

Dataset
Arabidopsis thaliana genes (TAIR10)
Filters
[None selected]
Attributes
Gene stable ID
Transcript stable ID

Dataset
[None Selected]

● **Features** ○ **Variant (Germline)**
○ **Structures** ○ **Sequences**
○ **Homologues**

⊞ GENE:

⊟ EXTERNAL:

GO
□ GO term accession
□ GO term name
□ GO term definition

PO
□ PO term accession (bp)
□ PO term name (bp)
□ PO term definition (bp)

GOSlim GOA
□ GOSlim GOA Accession(s)

External References (max 3)
□ ChEMBL ID
□ European Nucleotide Archive ID
□ Expression Atlas ID
□ INSDC protein ID
□ KEGG Pathway and Enzyme ID
□ MEROPS - the Peptidase Database ID
□ miRBase accession
□ miRBase ID
□ miRBase transcript name ID
□ NASC Gene ID
□ NCBI gene ID
□ PDB ID
□ Plant Reactome Pathway ID
□ Plant Reactome Reaction ID
□ Plant Structure Ontology ID
□ RefSeq DNA ID
□ RefSeq peptide ID
□ RFAM ID
□ STRING ID
□ TAIR ID
□ TAIR Gene Name ID
□ TAIR Locus (Model) ID
□ TAIR Translation identifier ID
□ tRNAScan-SE ID
□ UniGene ID
□ UniParc ID
□ UniProtKB/SpliceVariant ID
□ UniProtKB/Swiss-Prot ID
□ UniProtKB/TrEMBL ID

Name	Description
Variant Effect Predictor VEP	Analyse your own variants and predict the functional consequences of known and unknown variants via our Variant Effect Predictor (VEP) tool.
HMMER	Quickly search our genomes for your protein sequence.
BLAST/BLAT	Search our genomes for your DNA or protein sequence.
Assembly Converter	Map (liftover) your data's coordinates to the current assembly.
ID History Converter	Convert a set of Ensembl IDs from a previous release into their current equivalents.

Convert assembly-specific
&&
cross-reference gene IDs

Suggestions towards standardizing gene nomenclature

- Once the data is released from INSDC, everyone must use the same ID
- Prioritize representation of (up-to-date) proteomes in UniProt
- Gene IDs independent of assembly version, genomic location, function & orthology
- Adopt standards from good quality nomenclature systems (e.g., human, yeast, Arabidopsis)

Suggestions towards standardizing gene nomenclature

- Standard tools to convert IDs across resources, assemblies, etc.
- **Community collaborative platform** - Build a 'data wiki' and let communities provide their own names (Dan Bolser)

Gene Names: Ensembl gene name projection pipeline

- Up to 90% of gene names could be projected from closely related species (*e.g.* between the rice).
- For which pairs of species does it make sense to project genes between?
  - E.g. over what taxonomic range and with what stringency?

Gene Nomenclature Planteome Strategy

Pankaj Jaiswal
Oregon State University

September 5, 2018
AgBioData Group Meeting

Planteome

NSF #1340112

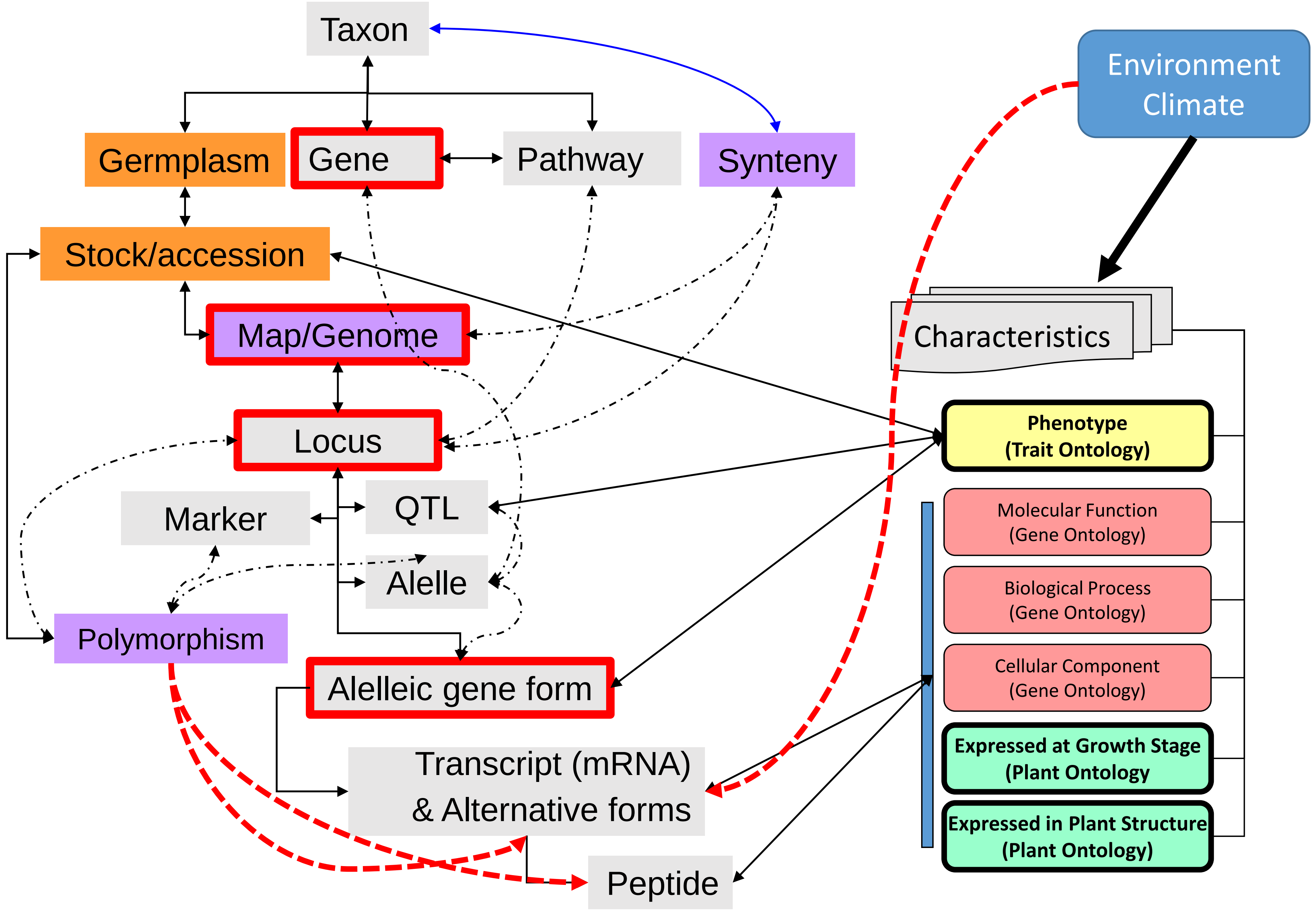
Genomes

- Reference genomes:
  - Accession/germplasm/ecotype-specific
- Non-reference genomes
  - For genetic diversity (Mainly for SNPs but if fully sequenced can be used for finding new and novel genes)
    - Accession/germplasm/ecotype-specific
- Pan-genomes
  - Species-level
  - Genus-level

Gene set changes observed

- Identify new gene (includes coding and noncoding)
- Identifying null allele (gene missing in an ecotype/accession)
- Existing genes
    - Start and stop coordinates may change
    - New/altered UTRs
    - Different transcript isoforms
        - Novel splicing
        - New transcribed region
        - New peptide
    - Mergers
    - Splits (may need adding a minimum of one new gene)
    - Obsolete/delete

Data and Biocuration


Taxon
Germplasm
Gene
Pathway
Synteny
Environment Climate
Stock/accession
Map/Genome
Characteristics
Locus
Phenotype (Trait Ontology)
Marker
QTL
Molecular Function (Gene Ontology)
Alelle
Biological Process (Gene Ontology)
Polymorphism
Alelleic gene form
Cellular Component (Gene Ontology)
Expressed at Growth Stage (Plant Ontology
Transcript (mRNA) & Alternative forms
Expressed in Plant Structure (Plant Ontology)
Peptide

Planteome

Some points to consider

- Need consistency for the community and semantic querying, NLP and data updates
- Keep the Super gene set at the Species/genus level considering we will see a lot of Pan-genome projects and germplasm-specific gene sets
- Populate the super gene set by adding uniques to the pool
- For each version of the annotation (not assembly) map to the super pool and borrow the IDs or create a new one for new genes
- Never create version dependent IDs or insert version# in gene ID
- Make an arrangement with INSDC/GenBank to deposit the new annotation (proteomes etc)—THEY WILL TAKE CARE OF THE MAPPING AND VERSION NUMBER as long as IDs are consistent.
    - MANY genomes lack/do not deposit annotations

Some points to consider

- If the users perform structural annotation to revise the existing model, continue using the same gene ID at the locus
  - Release it with the new annotation version periodically
  - Second/third party annotations: They need to map to the super set IDs and share their data to become part of the official release. EVERYONE Needs to use the same common set of updated gene sets.
- If a new gene is added, create a new ID
  - If the genome assembly is in the pseudomolecule form use the number series and zero padded 100/1000th space to maintain series
  - If the genome is in scaffolds use the next available number
  - Release it with the new annotation version periodically (quarterly/bi/annual)

Planteome