GOLDEN HELIX

Enabling Precision Medicine

# Genomic Prediction Methods

SNP & VARIATION SUITE

Darby Kammeraad - Field Application Scientist

CIOReview

20 most promising Biotech Technology Providers

pharma TECH OUTLOOK

Top 10 Analytics Solution Providers

Gartner

Hype Cycle for Life sciences

# Golden Helix – Who We Are

**Golden Helix is a global bioinformatics company founded in 1998.**

GlaxoSmithKline

varSEQ®

- Variant Calling
- Filtering and Annotation
- Clinical Reports
- CNV Analysis
- Pipeline: Run Workflows

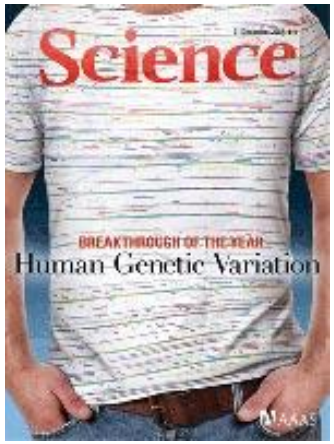
VARIANT WAREHOUSE

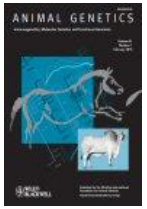
- Variant Warehouse
- Centralized Annotations
- Hosted Reports
- Sharing and Integration

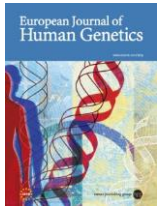
SNP & VARIATION SUITE

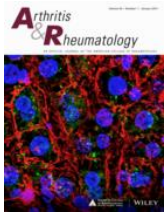
- GWAS
- Genomic Prediction
- Large-N-Population Studies
- RNA-Seq
- Large-N CNV-Analysis

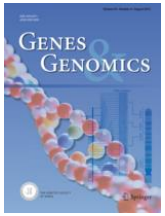
# Cited in over 1100 peer-reviewed publications







# Over 350 customers globally

SickKids
THE HOSPITAL FOR SICK CHILDREN

Cincinnati Children's
Hospital Medical Center

The Children's Hospital of Philadelphia

Stanford University

UBC

Ucla

Yale

The Feinstein Institute for Medical Research
North Shore-Long Island Jewish Health System

North Shore LIJ

PREVENTION GENETICS
DISEASE PREVENTION THROUGH GENETIC TESTING

MAYO CLINIC

LINEAGEN

MOFFITT CANCER CENTER

Dartmouth-Hitchcock
NORRIS COTTON CANCER CENTER

BAYER

Lilly

abbvie

TEVA

NATIONAL CANCER INSTITUTE

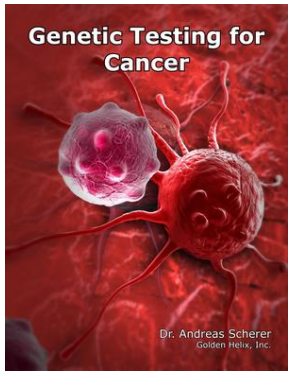
USDA
USDA Agricultural Research Service

FDA

# Golden Helix – Who We Are

**When you choose a Golden Helix solution, you get more than just software**

- REPUTATION
- TRUST
- EXPERIENCE

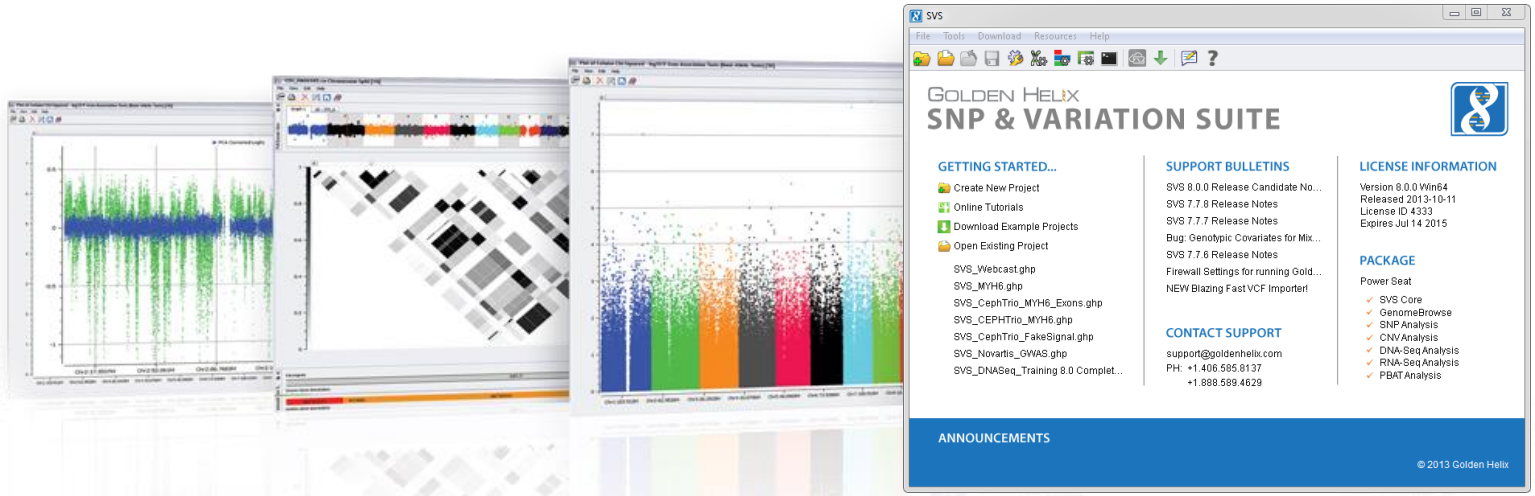



- INDUSTRY FOCUS
- THOUGHT LEADERSHIP
- COMMUNITY

- TRAINING
- SUPPORT
- RESPONSIVENESS

- INNOVATION and SPEED
- CUSTOMIZATIONS

# SNP & Variation Suite (SVS)




## Core Features

- Powerful Data Management
- Rich Visualizations
- Robust Statistics
- Flexible

## Applications

- Genotype Analysis
- DNA sequence analysis
- CNV Analysis
- RNA-seq differential expression

# Approximate Agenda

| | |
|---|---|
| 1 | Genomic Prediction |
| 2 | K-fold Cross Validation |
| 2 | Example project in SVS |
| 3 | Use Case – Beef palatability |

# Background

- **Genomic prediction is a key focus for agrigenomics**
- **Growing world population requires improved food production**
  - 3B in 1960
  - 7.5B today
  - 9.7B projected in 2050

Source: Wikipedia

| Country | Population 2010 | Population 1990 | Growth (%) 1990–2010 |
|---|---|---|---|
| *World* | 6,895,889,000 | 5,306,425,000 | 30.0% |
| China | 1,341,335,000 | 1,145,195,000 | 17.1% |
| India | 1,224,614,000 | 873,785,000 | 40.2% |
| United States | 310,384,000 | 253,339,000 | 22.5% |
| Indonesia | 239,871,000 | 184,346,000 | 30.1% |
| Brazil | 194,946,000 | 149,650,000 | 30.3% |
| Pakistan | 173,593,000 | 111,845,000 | 55.3% |
| Nigeria | 158,423,000 | 97,552,000 | 62.4% |
| Bangladesh | 148,692,000 | 105,256,000 | 41.3% |
| Russia | 142,958,000 | 148,244,000 | -3.6% |
| Japan | 128,057,000 | 122,251,000 | 4.7% |

# Why Use Genomic Prediction?

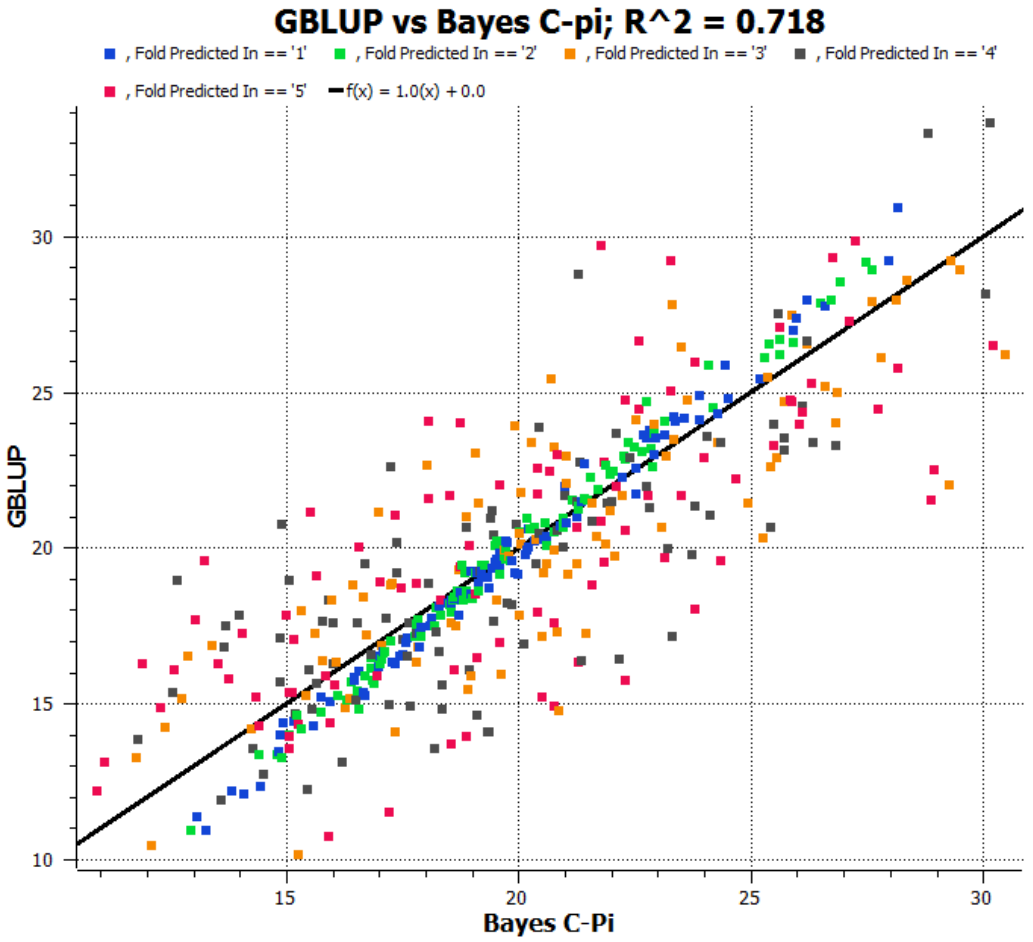
- **Calculate breeding value (gEBV) for all subjects in a population**
  - May be more accurate than breeding selection based only on pedigree and trait data
- **Predict breeding values for subjects with unknown phenotypes**
  - May avoid costly and lengthy field trials
  - May not always be possible to measure the phenotype
- **Identify genetic markers with best predictive power for a trait**
  - Assist in development of predictive tests and other assays

OR

?

# Genomic Prediction Methods Available in SVS

- **3 methods available**
  - GBLUP (Genomic Best Linear Unbiased Predictor)
  - Bayes C
  - Bayes C-pi



# GBLUP

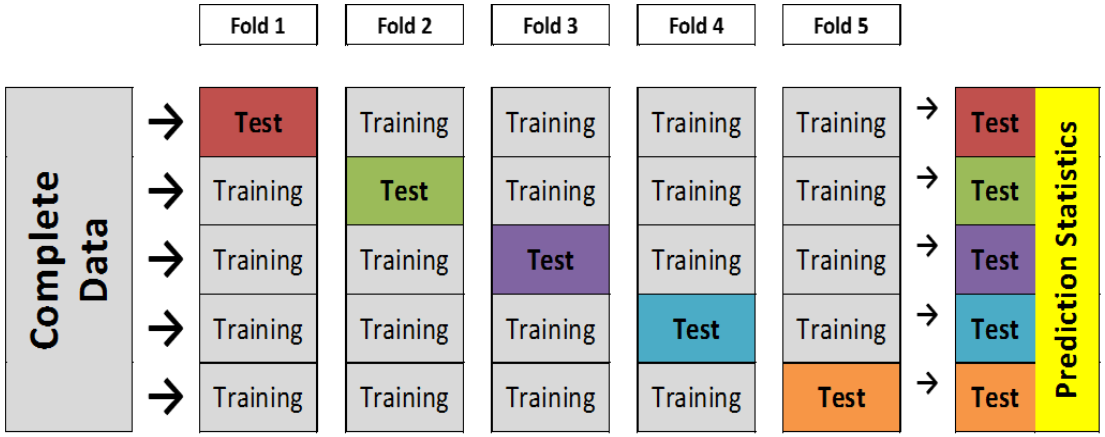
- **Assumes all loci contribute to phenotype**
- **Incorporates genomic relationship matrix in mixed linear model framework to account for relatedness among samples**
- **Calculates allele substitution effect for each SNP**
- **Computes estimated breeding values and predicted phenotypes for all samples**
- **Also calculates:**
  - Pseudo-heritability of trait
  - Genetic component of trait variance
  - Error component of trait variance
  - New GCTA methods (correct for environmental interactions)
    - Yang J, et al (2011) 'GCTA: A Tool for Genome-wide Complex Trait Analysis'. Am J Hum Genet 88, pp. 76-82.

# Bayes C, C-pi

- Bayesian methods predict effects of loci together with parameters required to define probability distribution over effects
- Gibbs sampling Markov Chain Montey Carlo used to obtain parameter estimates
- The π (pi) parameter is the prior probability that any SNP will have no effect.
- Pi is fixed in Bayes C, Bayes C Pi is considered unknown and allowed to vary
- Both methods return allele substitution effect, breeding value, other parameters of final model
- SVS implementation incorporates genomic relationship matrix

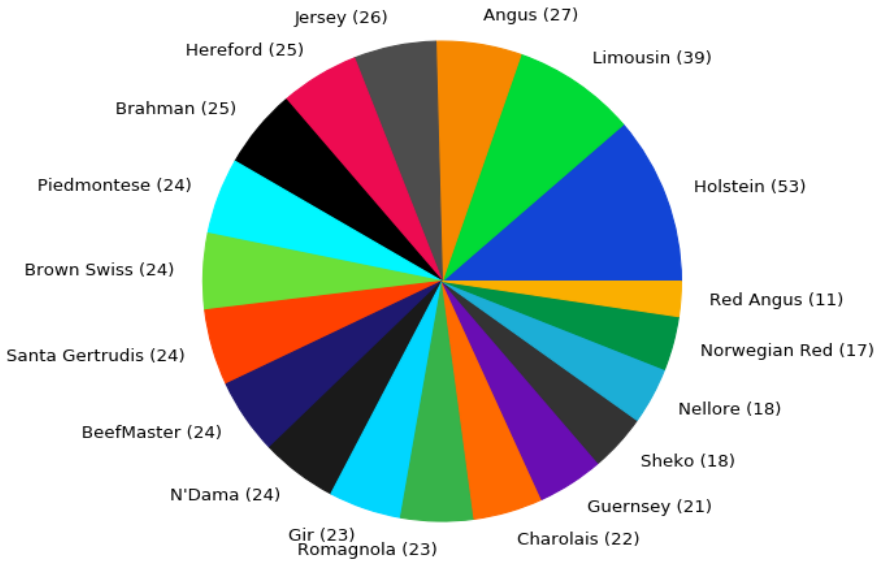
# K-Fold Cross-Validation

- Build a model that can be applied to new genetic data to predict a phenotype
- Cross Validation makes it possible to assess the performance built from a given reference/training dataset.
- Can be used with GBLUP, Bayes C, Bayes C-pi
- Requires all samples have a phenotype value
- Can include covariates



# Simulated Cattle Data

- **354 Bos taurus cattle from Bovine HapMap project**
  - 300 samples: training set
  - 54 samples: validation set (no phenotypes)
- **Illumina 50k genotypes**



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# SNP & VARIATION SUITE

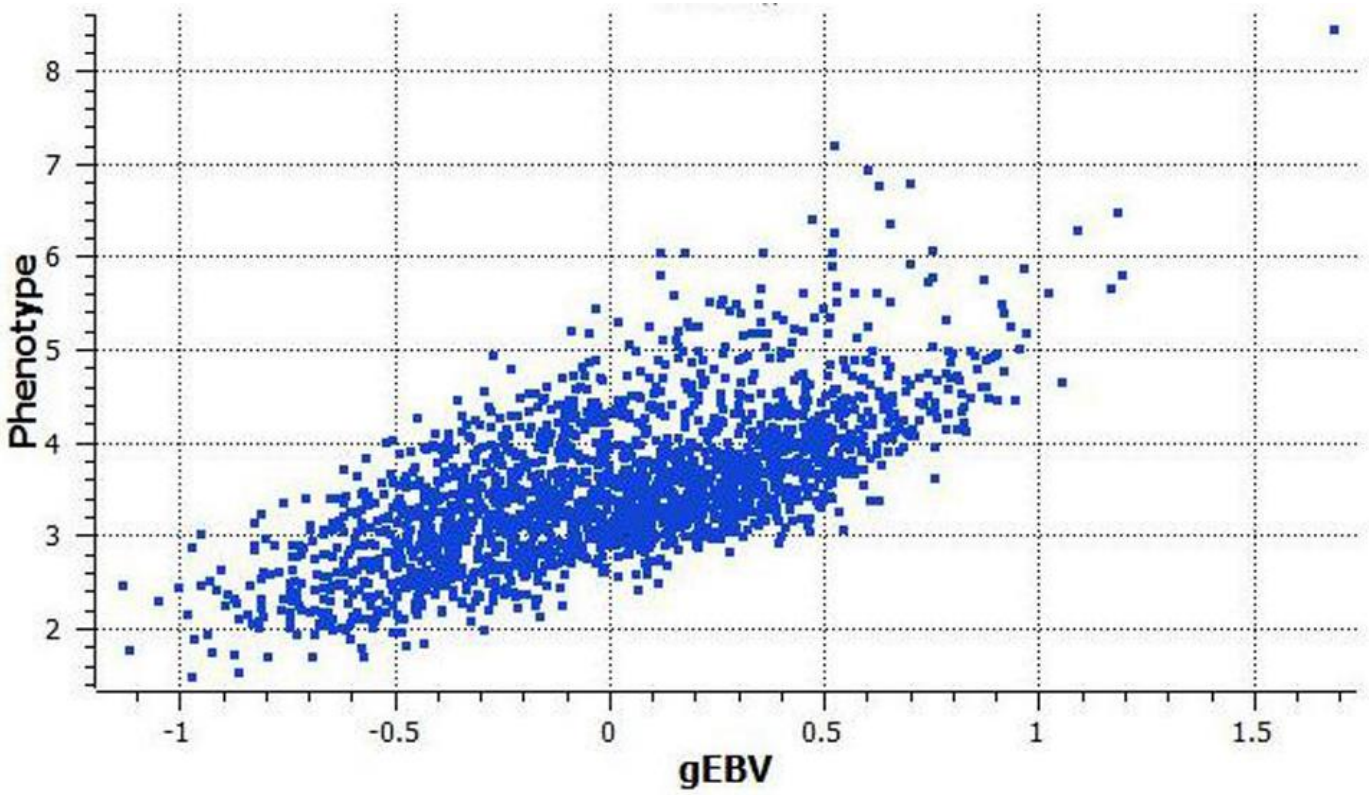
# Use Case – Improving Beef Quality

- **Dr. Raluca Mateescu**
  - Department of Animal Sciences at University of Florida
  - Journal of Animal Science 90, 4248-4255 (2012)
    - Link to slides http://goldenhelix.com/media/pdfs/webcasts/GoldenHelix_July2015_Handout.pdf
    - Link to webcast https://www.youtube.com/watch?v=e6Czycr_DnE

- **Develop tools to select for:**
  - Nutritious & tasty beef
    - **WB-Steak Shear Force**
    - Tenderness
    - Juiciness
    - Connective tissue
    - Beef Flavor
  - Improved production

# Use Case – Output from GBLUP

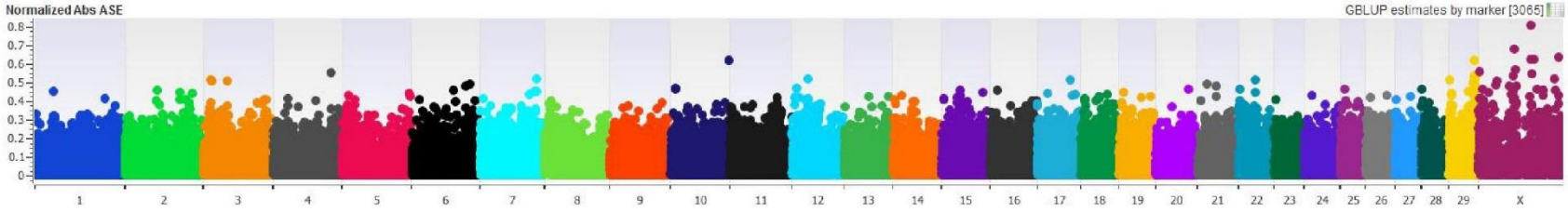
- **Correlations for Shear Force**
  - Actual phenotypes vs Estimated Breeding value (gEBV)



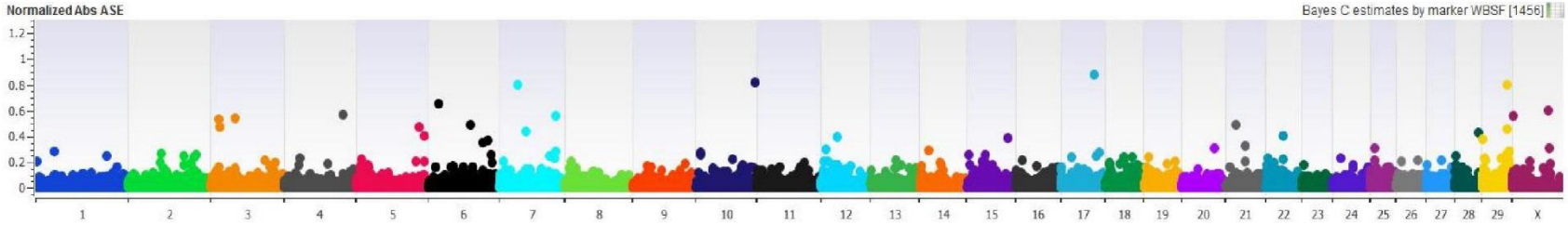
# Use Case – Improving Beef Quality

- **Genomic Prediction results – Shear Force**
  - GBLUP and Bayes C-pi
  - Manhattan plot with Allele Substitution Effects

GBLUP




Bayes C-pi

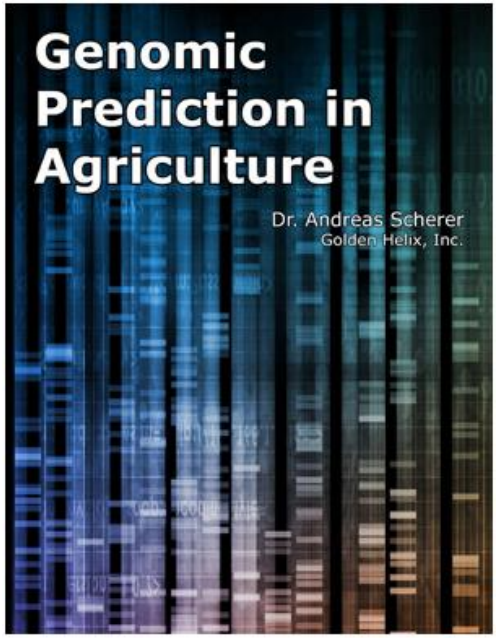


# Use Case – Success

- **Outcome of the study**
  - Identified markers associated with beef quality
    - *SAPS3*: modulates protein phosphatase catalytic subunits
    - *CAPN1*: modulates proteolysis of cytoskeletal remodeling and signal transduction
    - *CHI3L2*: involved in cartilage biogenesis
    - *CA10*: catalyzes reversible hydration of carbon dioxide
    - *GPHN*: involved in membrane protein-cytoskeleton interactions

# Additional Information

- **Genomic Prediction eBook**
- **Golden Helix at PAG 2018 – San Diego!**
  - Grand Exhibit Hall
  - Come see demos and ask us questions!
- **SVS package upgrade!**
  - NGS-based CNV calling for large sample size & association tests
- **SVS End of Year Pricing Bundles**
  - SVS Single User License - $2,995
  - SVS/VarSeq Bundle - $7,995
  - SVS Imputation Module (2 User License) - $7,995



# Questions or more info:

- Email info@goldenhelix.com
- Request an evaluation of the software at www.goldenhelix.com
- Check out our abstract competition!