

Monitoring Automated Genetic Diagnostic Laboratories

Ben Miller & Larry Shatzer

Myriad Genetics

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splunk >

Disclaimer

During the course of this presentation, we may make forward looking statements regarding future events or the expected performance of the company. We caution you that such statements reflect our current expectations and estimates based on factors currently known to us and that actual events or results could differ materially. For important factors that may cause actual results to differ from those contained in our forward-looking statements, please review our filings with the SEC. The forward-looking statements made in the this presentation are being made as of the time and date of its live presentation. If reviewed after its live presentation, this presentation may not contain current or accurate information. We do not assume any obligation to update any forward looking statements we may make. In addition, any information about our roadmap outlines our general product direction and is subject to change at any time without notice. It is for informational purposes only and shall not, be incorporated into any contract or other commitment. Splunk undertakes no obligation either to develop the features or functionality described or to include any such feature or functionality in a future release.

About Ben

- **Myriad:**

- Operational Intelligence, Dec 2015-Present

- Process Engineering, 2009-2015

- Technical Development, 2008-2009

- **Prior:**

- Technical Support, Applications for Velocity11

- Automation Intern, GlycoFi

- MS Genetic Engineering, Dartmouth College

- **Hobbies:**

- Biking

- Skiing

- Climbing

-  bentonmiller

-  bentonjmiller



About Larry



- Been at Myriad for 7.5 years
- Configuration/Release Management, and a developer in previous life
- Contributor to various open source projects
- Has expensive hobbies (3D printing, laser cutting, photography, board games)
- Father of 4

 lshatzer

 lshatzer

 larryshatzer

Butter-CUP!



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Agenda

- About Myriad Genetics
- Automated Genetic Testing
- History of Splunk at Myriad
- Tackling Problems
- Lessons Learned
- What's next for Splunk at Myriad

About Myriad Genetics



Just a few regulations...



Clinical
Laboratory
Improvement
Amendments





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Integrated BRACAnalysis[®] with Myriad myRisk[™] Hereditary Cancer

myRisk Genetic Result

RECEIVING HEALTHCARE PROVIDER	SPECIMEN	PATIENT	PATIENT
Physician Name, MD Michael Chouhan, FRCPC 300 Victoria Park Salt Lake City, UT 84143	Specimen Type: Blood Date Recd: Apr 8, 2012 Accession Date: Apr 8, 2012 Report Date: Apr 30, 2012	Name: June 12, 1959 Date of Birth: 1144 Patient ID: Female Accession #: 0008144-BLD Registration #: 000000	Physician Name: June 12, 1959 1144 Female 0001144-BLD 000000

RESULT: POSITIVE—CLINICALLY SIGNIFICANT MUTATION IDENTIFIED

Note: "CLINICALLY SIGNIFICANT" as defined in this report, is a genetic change that is associated with the presence of other medical interventions.

GENE	DESCRIPTION	INTERPRETATION
BRCA1	c.68_E8del (p.Glu2756A>T) Metagenomic	HIGH CANCER RISK This patient has Hereditary Breast and Ovarian Cancer (HBOC) syndrome.

DETAILS ABOUT BRCA1 c.68_E8del (p.Glu2756A>T): NM_021908.4, AKA: 167494AG

Functional Significance: Deletions - Abnormal Protein Production and/or Function
The heterozygous germline BRCA1 mutation c.68_E8del is predicted to result in the premature truncation of the BRCA1 protein at amino acid position 68 (p.Glu2756A>T).

Clinical Significance: High Cancer Risk
This mutation is associated with increased cancer risk and should be regarded as clinically significant.

ADDITIONAL FINDINGS: VARIANTS OF UNCERTAIN SIGNIFICANCE (VUS) IDENTIFIED	INTERPRETATION
GENE: CNM2NA (p.M99K) + 27A	UNCERTAIN CLINICAL SIGNIFICANCE There are currently insufficient data to determine if these variants cause increased cancer risk.

Additional Details About CNM2NA (p.M99K): The heterozygous germline CNM2NA (p.M99K) variant + 27A is located within the CNM2NA 5'UTR gene transcribed from the 5' end and is predicted to result in abnormal protein translation. Data indicate mutations are known to disrupt normal initiation of protein synthesis and are interpreted as pathogenic according to the recommendations of the American College of Medical Genetics (ACMG) et al. Genet Med. 12:208-205, 2008. However, an alternative to frame maintenance is located 8 genes acids downstream of the normal start codon. If this methionine were to be utilized as an alternative initiation codon, it would result in the deletion of the first 8 amino acids of the CNM2NA p.M99K protein. At this time, there is insufficient information to determine whether or not this alternative methionine is utilized, and if the resulting shortened protein would be fully functional.

Details About Non-Clinically Significant Variants: All individuals carry DNA changes (e.g., variants and most variants do not increase an individual's risk of cancer or other diseases. When identified, variants of uncertain significance (VUS) are reported. Likely benign variants of Poor Polymorphism and benign variants (Polymorphism) are not reported and available data indicate that these variants most likely do not cause increased cancer risk. Present evidence does not suggest that non-clinically significant variant findings be used to modify patient medical management beyond what is indicated by the personal and family history and any other significant clinical findings.

Variant Classification: Myriad's myRisk[™] Variant Reclassification Program continuously performs ongoing evaluations of variant classifications. In certain cases, healthcare providers may be notified for more clinical information or to arrange family testing to aid in variant classification. When new evidence about a variant is identified and determined to result in clinical significance and management change, that information will automatically be made available to the healthcare provider through an annotated report.

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myRisk Genetic Result Page 1 of 2

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myRisk Genetic Result Page 1 of 1

The genetic test result

The genetic test result indicates whether a clinically actionable mutation is identified from the 25 genes analyzed.

If positive, the genetic mutation is detailed with appropriate nomenclature, and its clinical and functional significance.

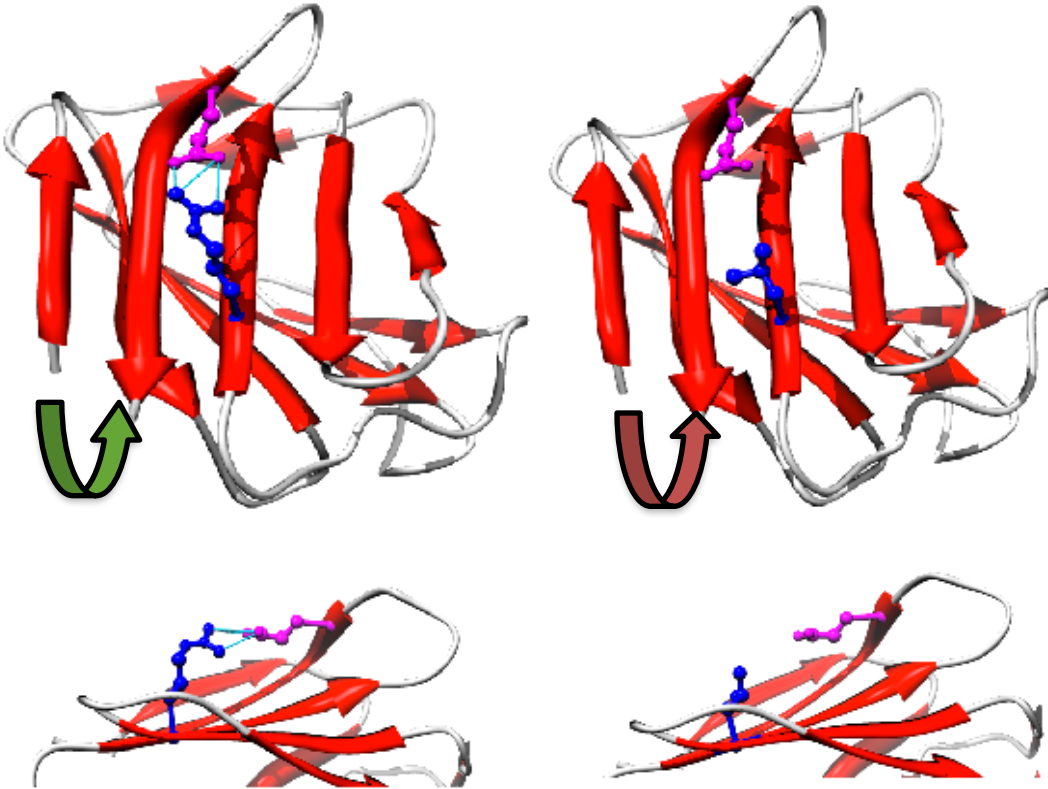
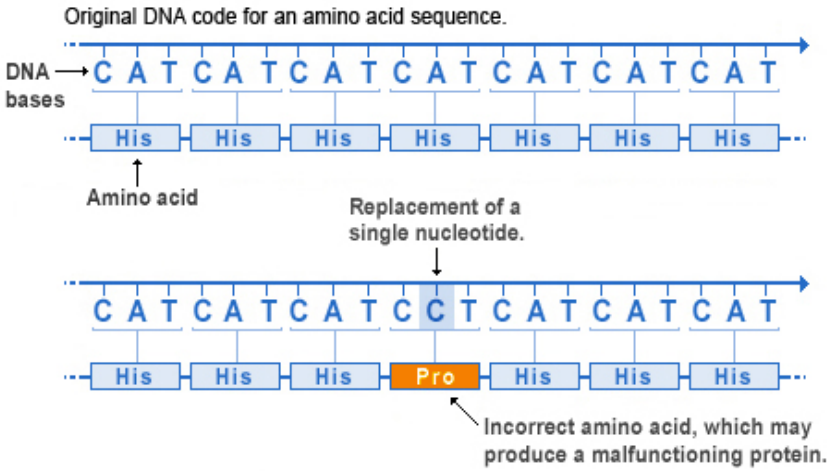
Presence of genetic variants of uncertain significance (VUS) that are not currently considered clinically actionable, are reported.

How do we do that?



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Missense mutation



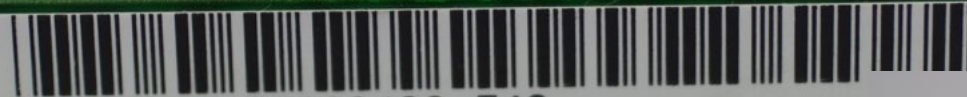
U.S. National Library of Medicine

How do we do that?



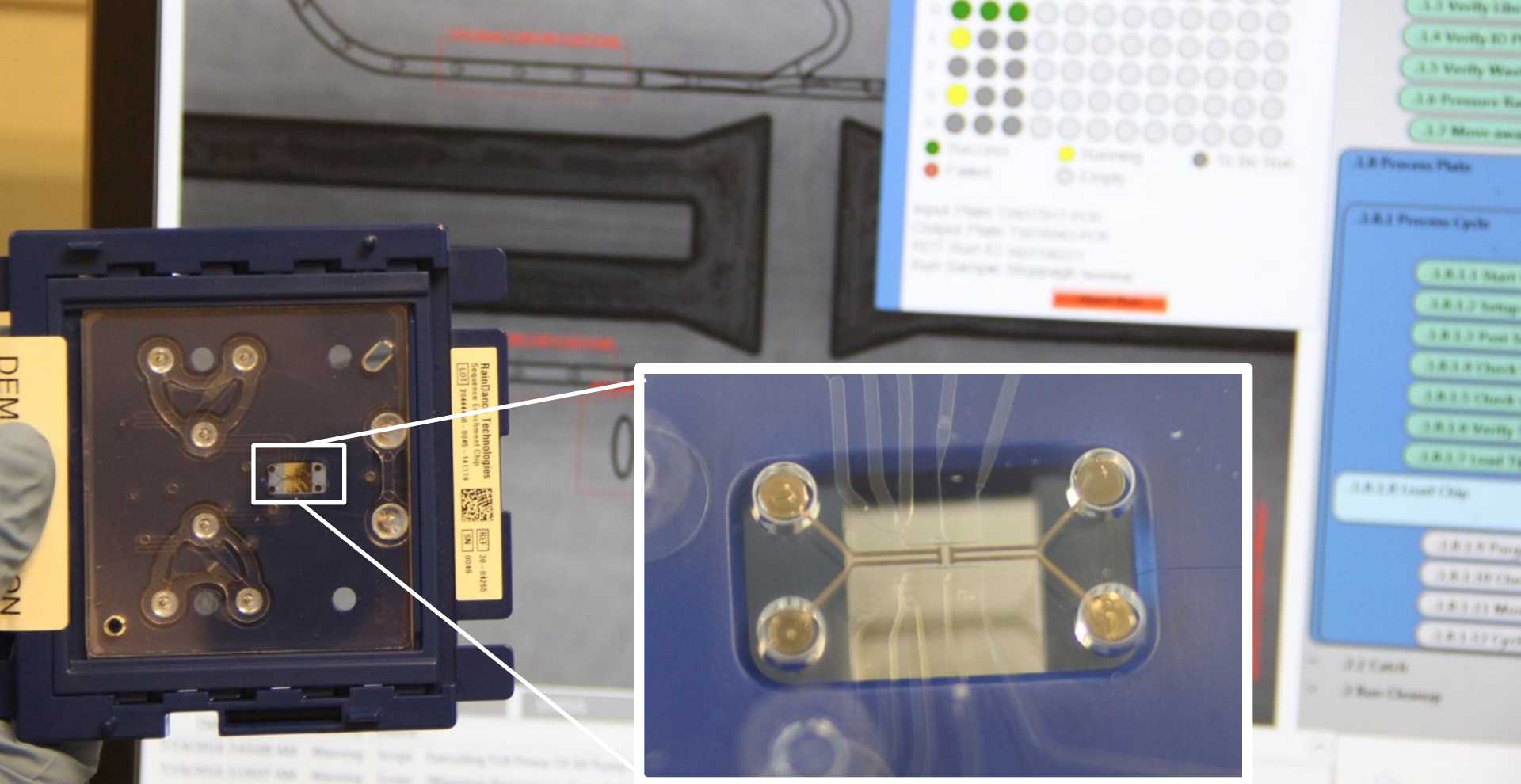
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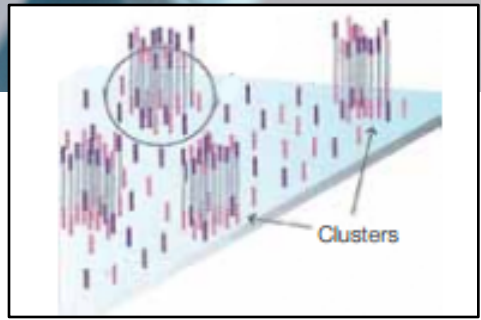
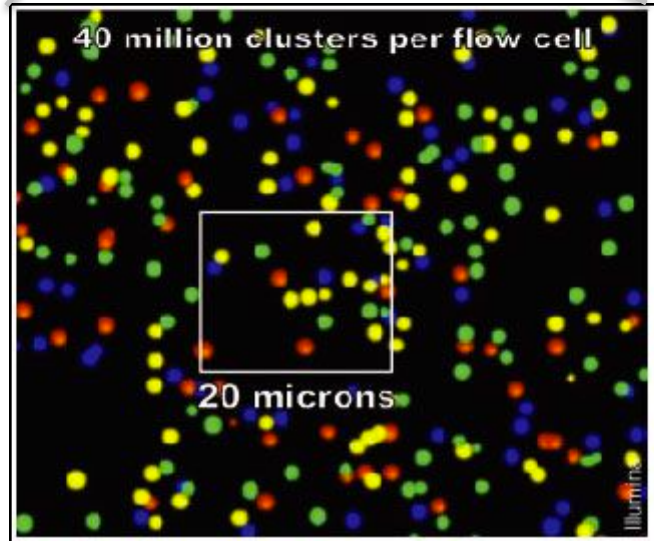
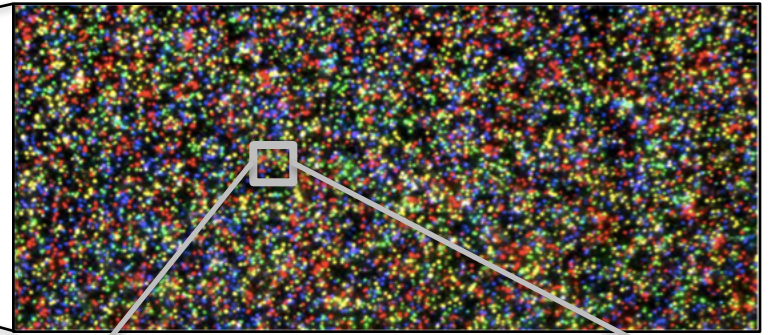
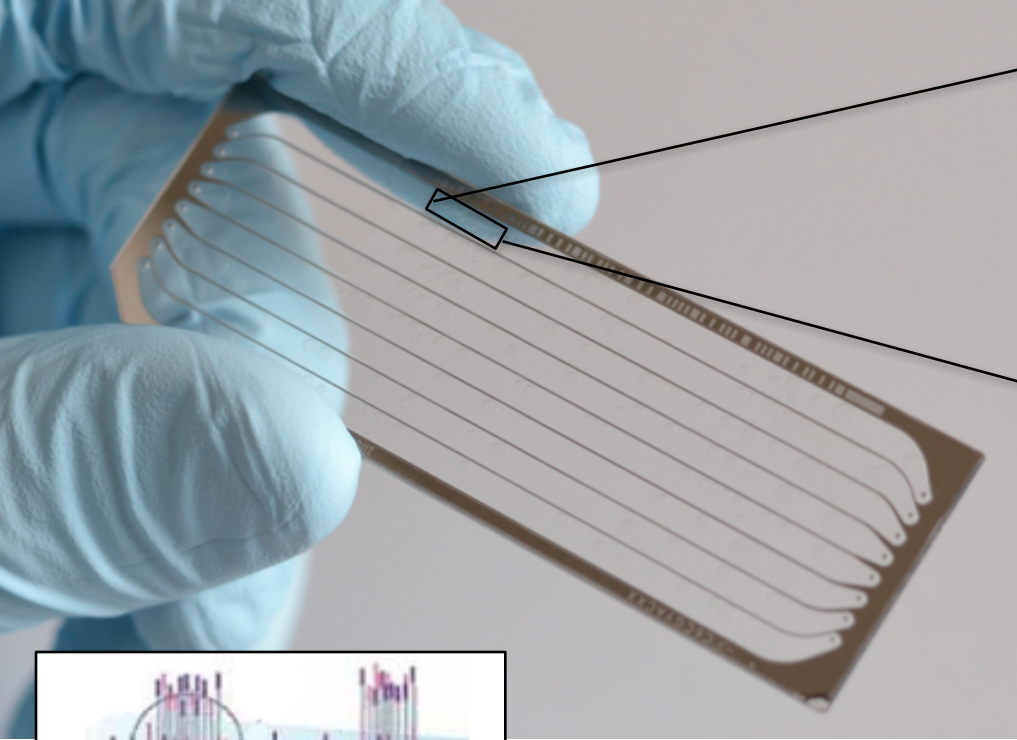
With Robots.



C0008488 - F48



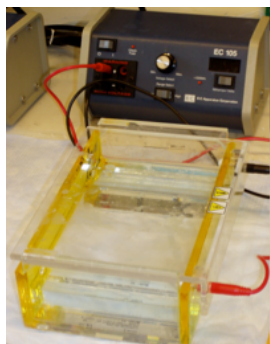




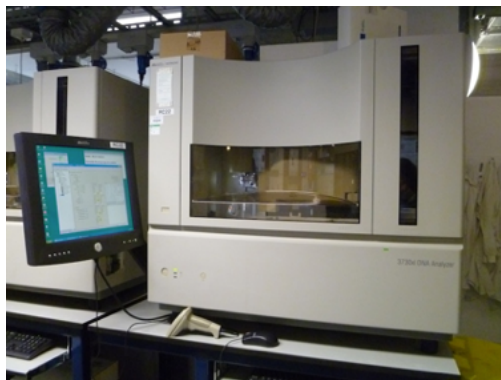
100's of systems to monitor



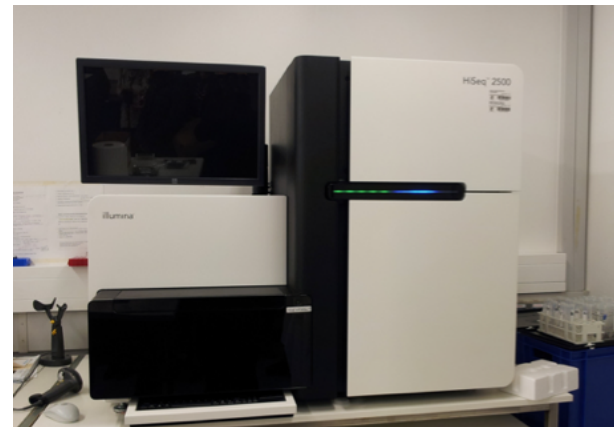
Technology changes fast



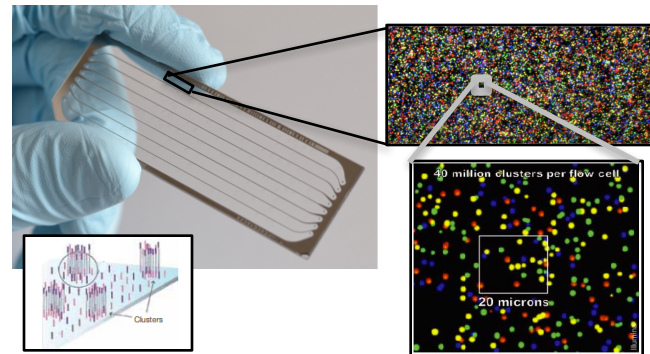
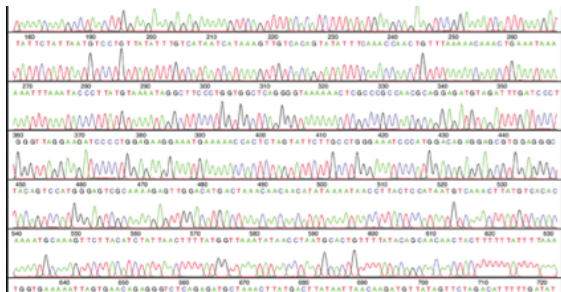
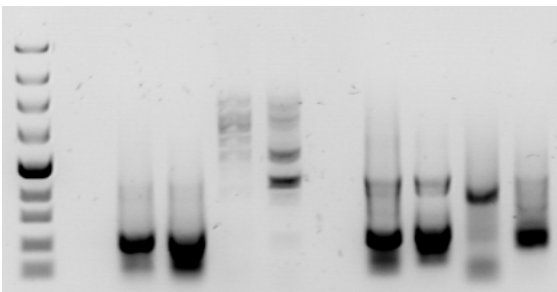
1985



2000

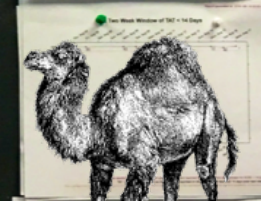
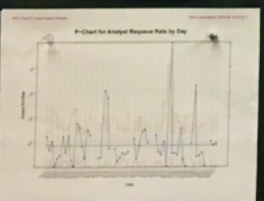
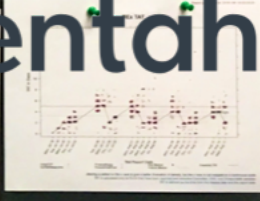
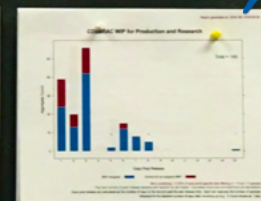
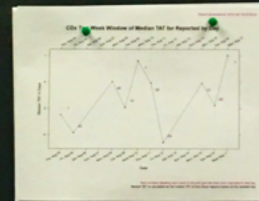
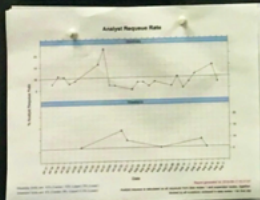
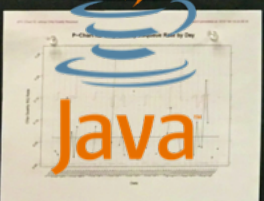
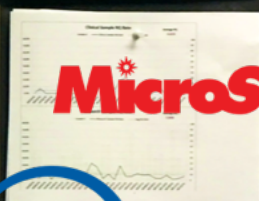
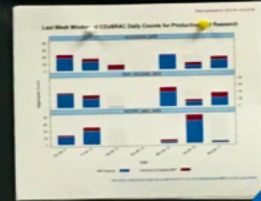
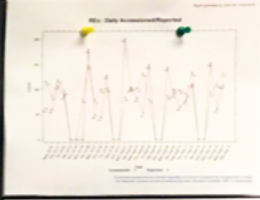
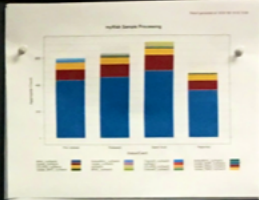
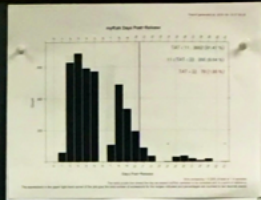


2015



History of Splunk at Myriad





Why Splunk?



Interactive Dashboards



Timely Alerts



Scheduled Reports



Variety of inputs

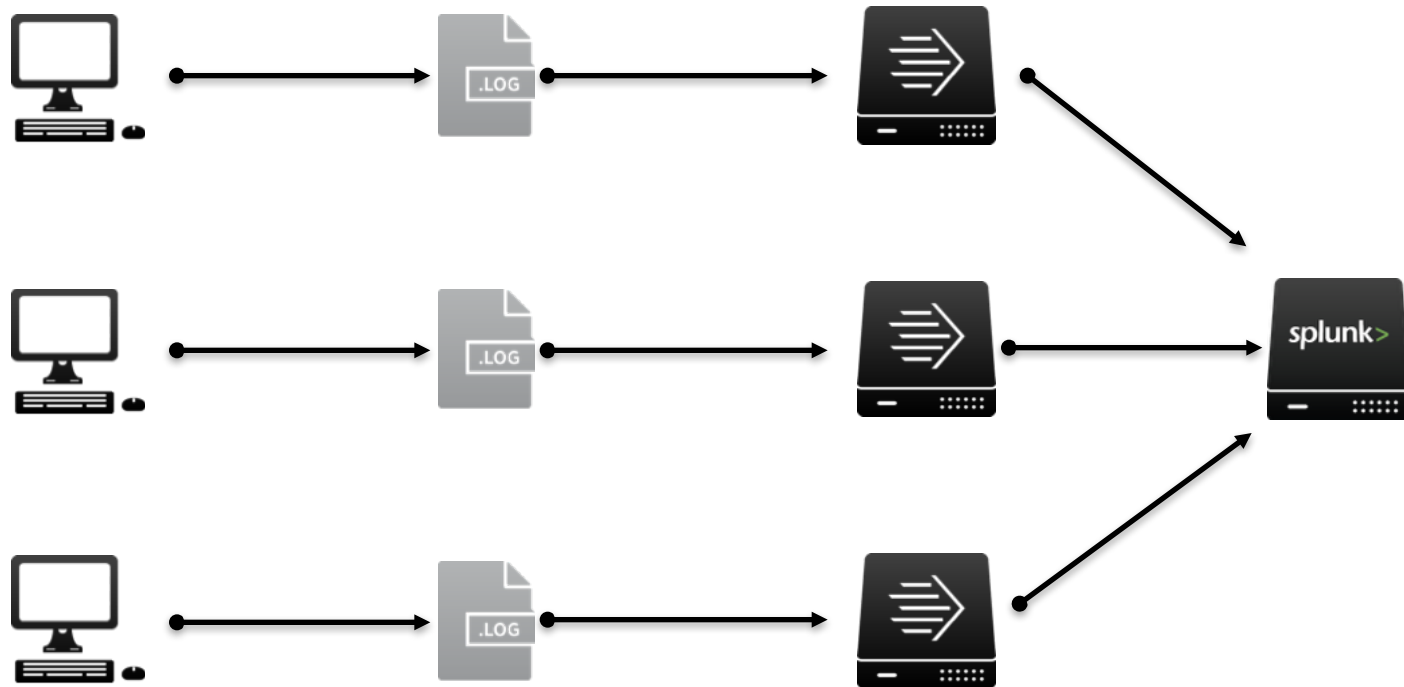
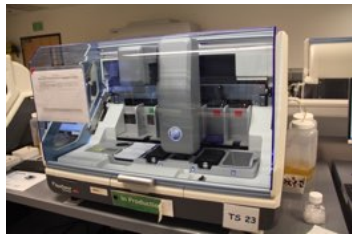


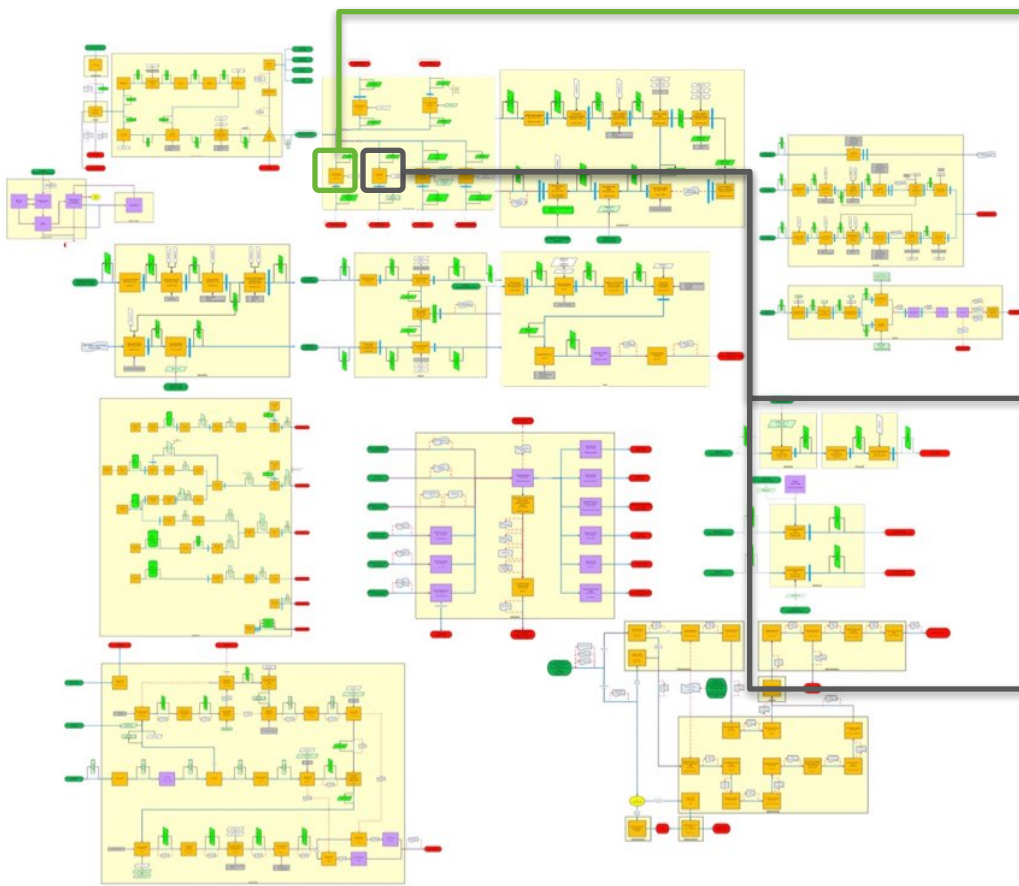
Rapid prototyping



Single portal for users

Splunk Deployment



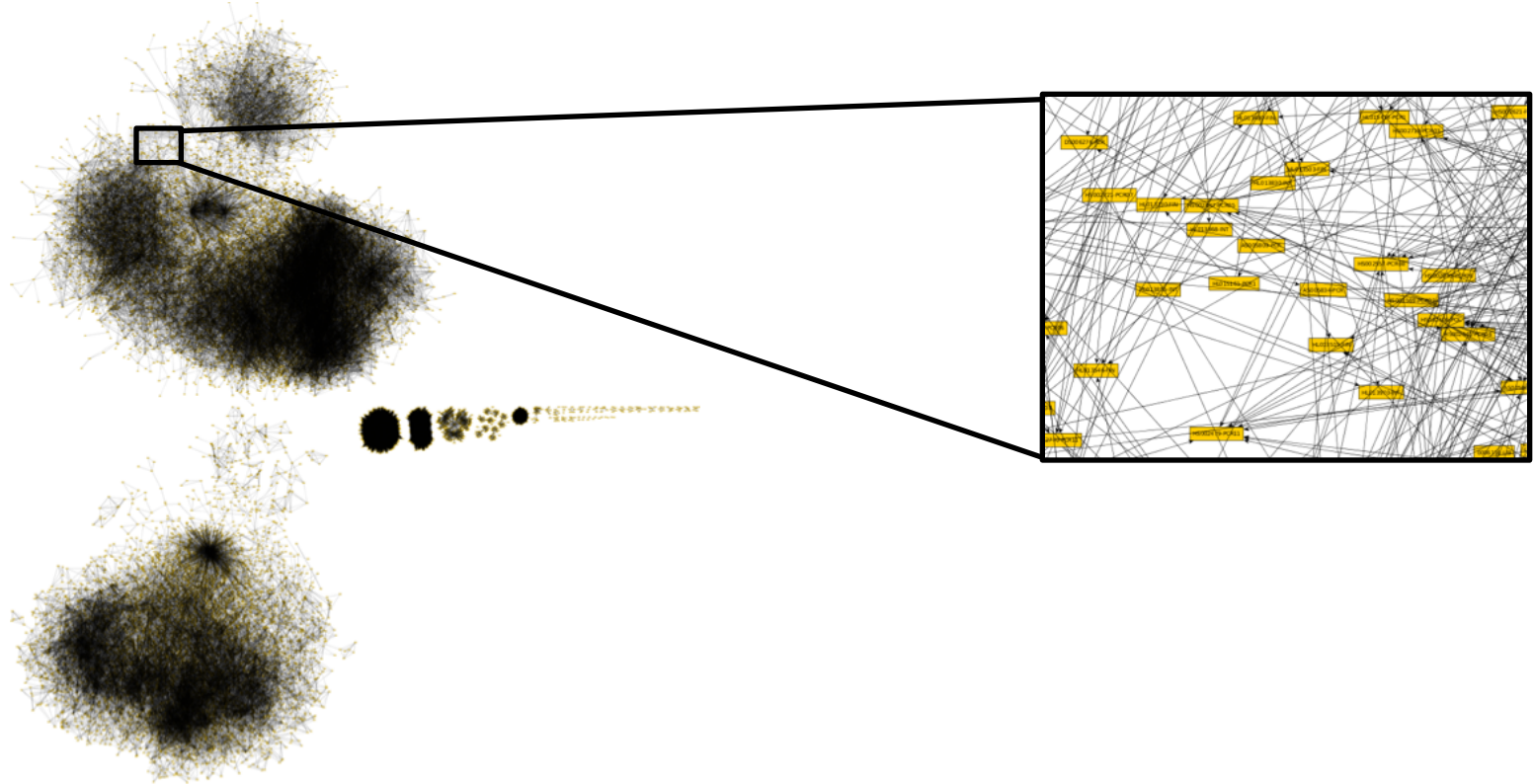


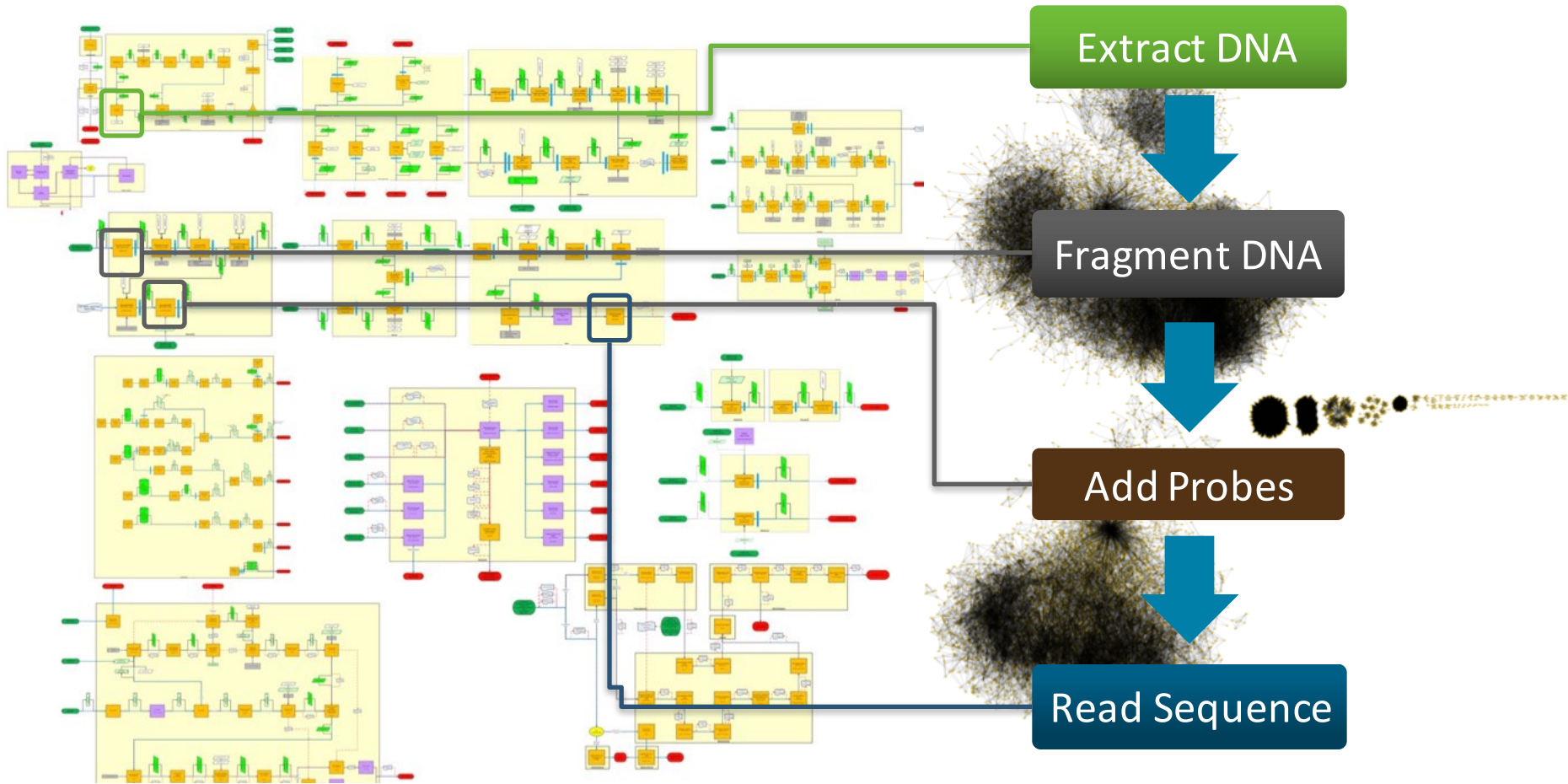
```
[2016-07-27 11:58:22,936] <request>
<transaction>Inoc Plates</transaction>
<user>bmiller</user>
<plates>
<plate>AM123456-DNA</plate>
<plate>TSI017803-PCR</plate>
<plate>TSI017804-PCR</plate>
<plate>TSI017805-PCR</plate>
<plate>TSI017806-PCR</plate>
</plates>
...
```

```
[2016-07-27 13:58:22,936] <request>
<transaction>Run Thunderstorm</transaction>
<user>lshatzer</user>
<plates>
<plate>TSI017803-PCR</plate>
<plate>TS017132-PCR</plate>
</plates>
...
```

```
[2016-07-27 13:52:12,236] <request>
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<user>lshatzer</user>
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<plate>TSI017804-PCR</plate>
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</plates>
```

Big ball of string...





Tackling Cultural Problems



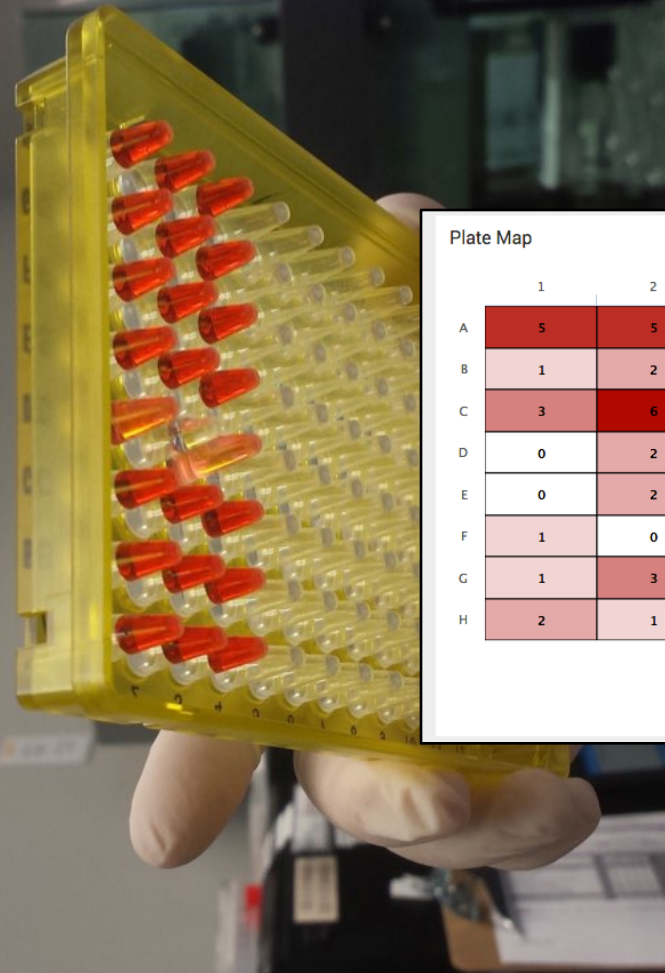
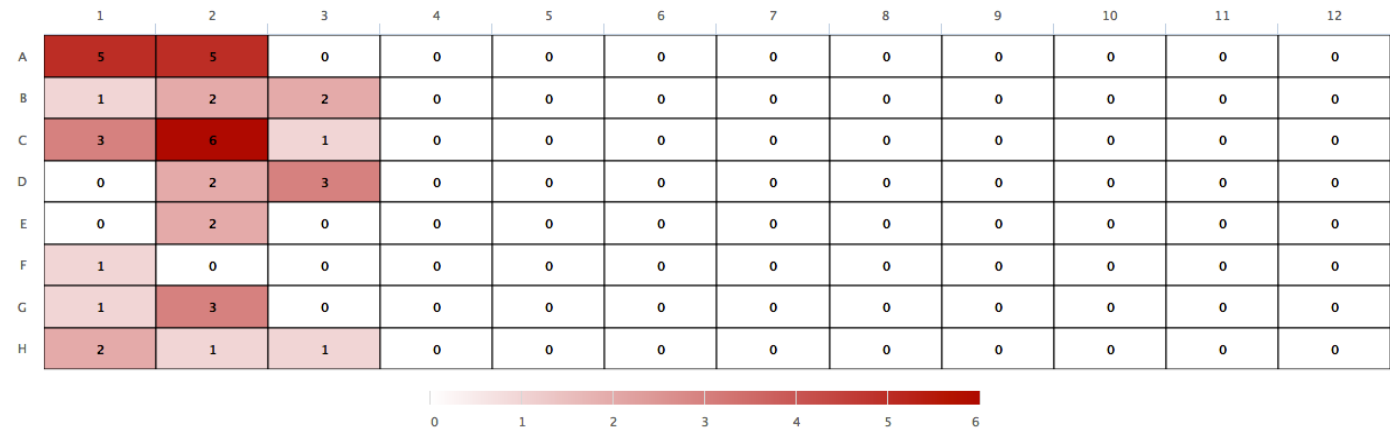
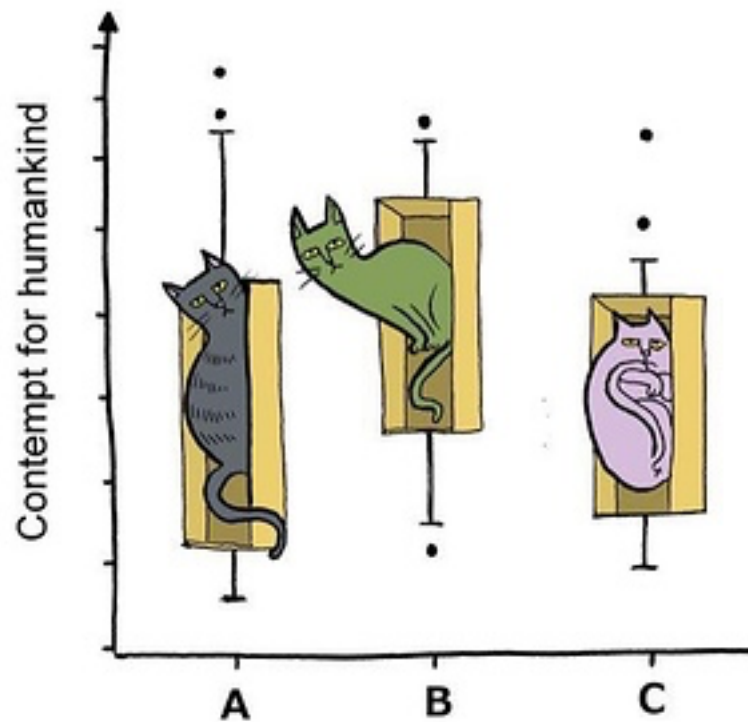


Plate Map

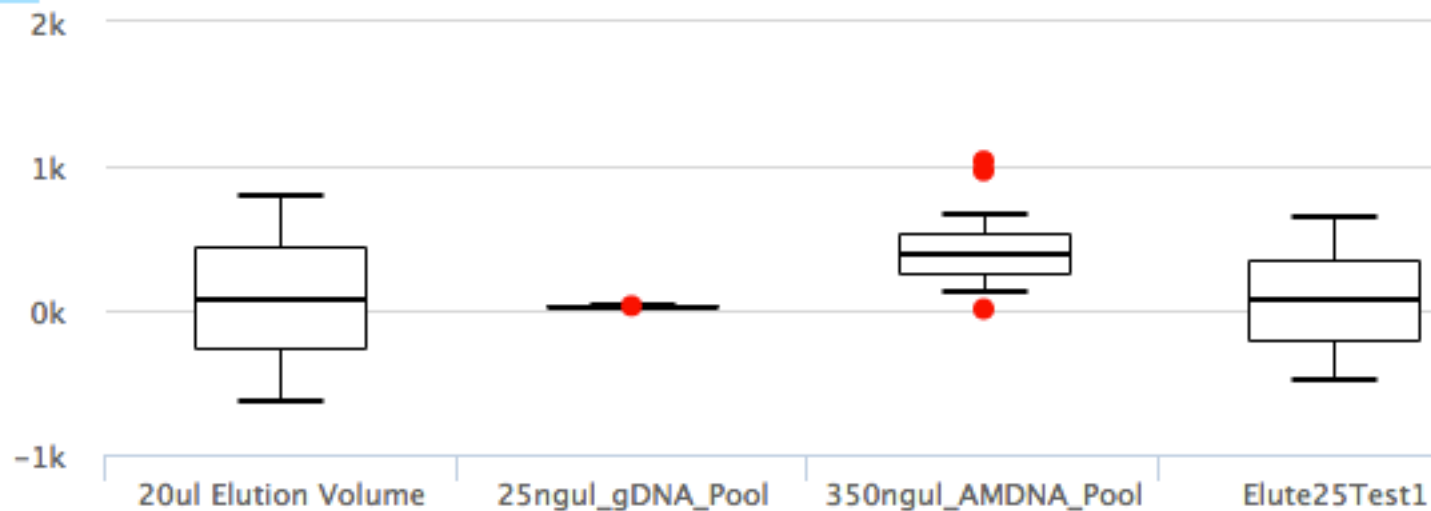


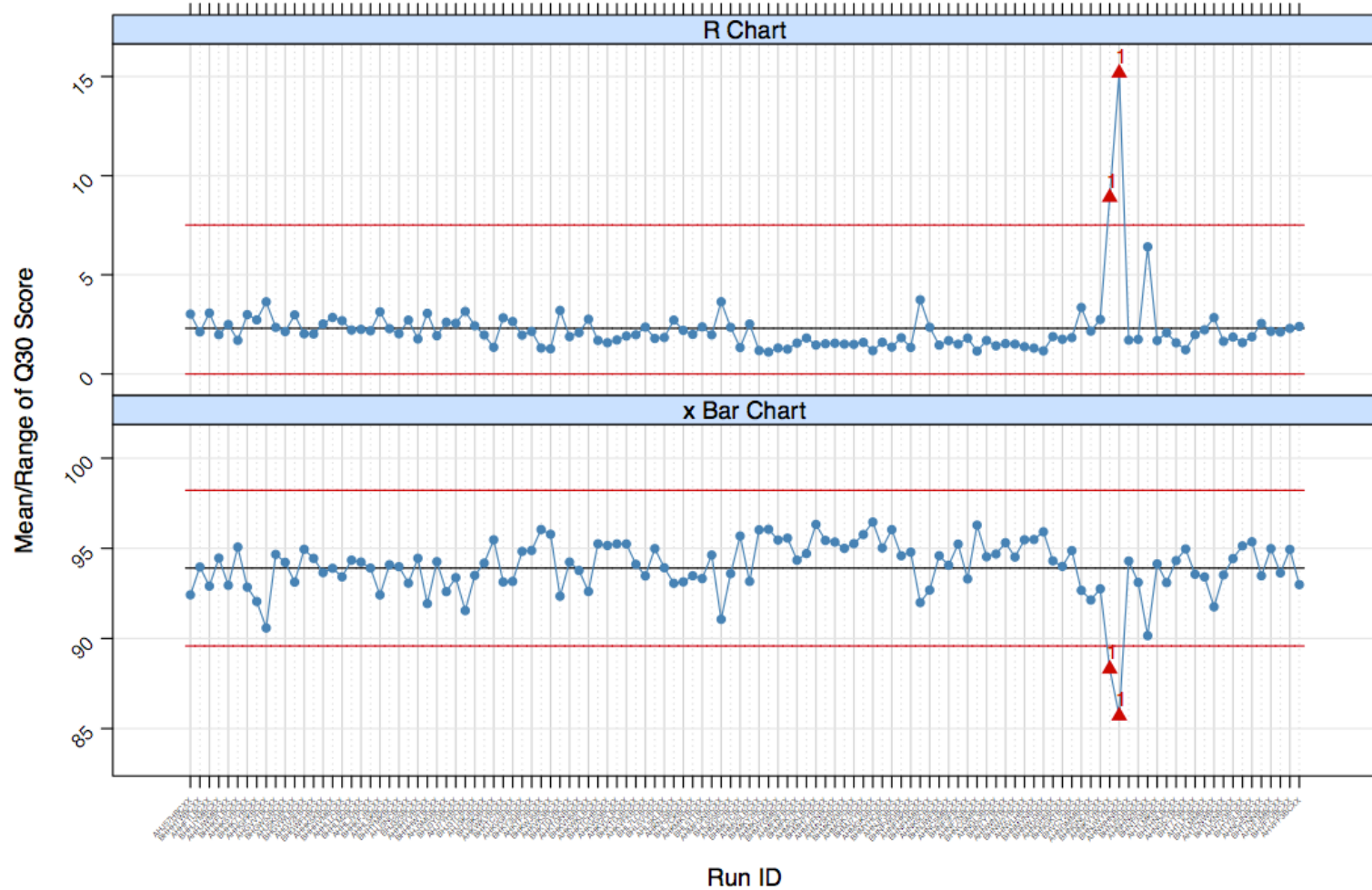
Box-and-Whisker Plot



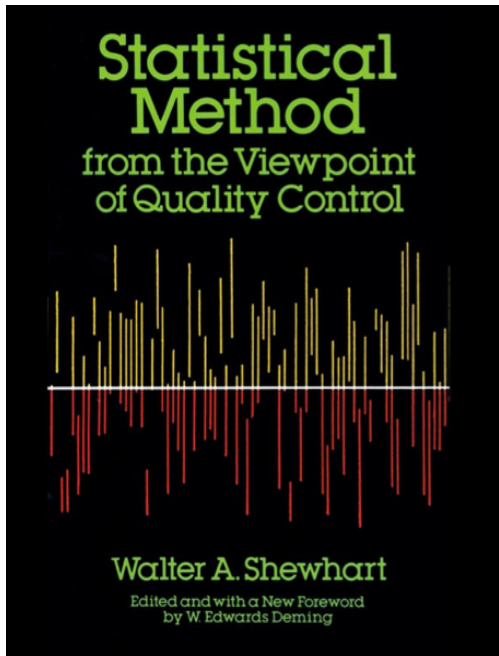
facebook.com/pedromics

Concentration Box-Plot by Source_Plate





Statistical Process Control



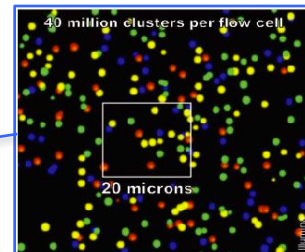
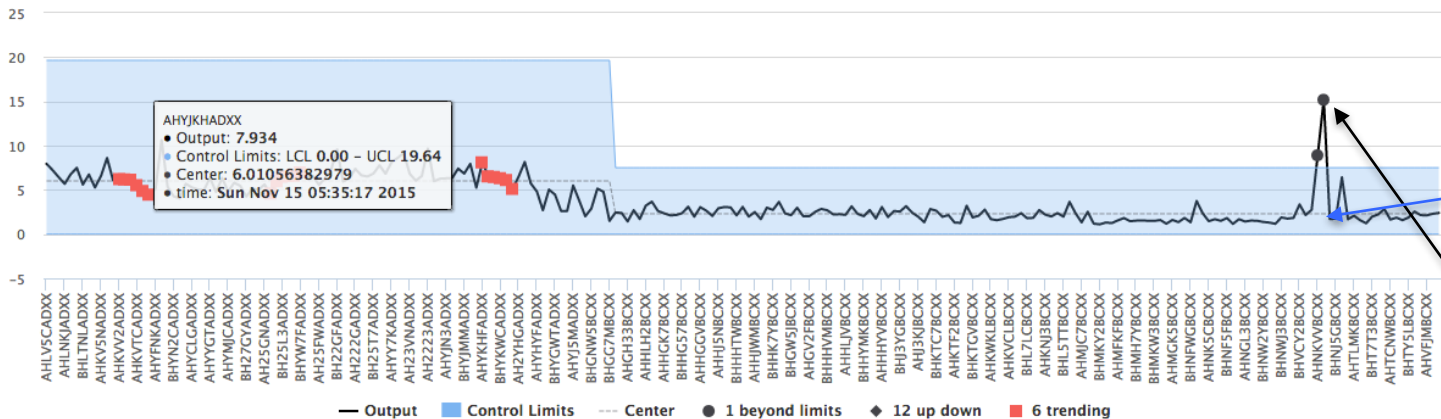
1. Origins:

- 1920's Pioneered at Bell Labs by Walter A. Shewhart
- Bell, AT&T, and US munitions manufacturers reduce waste due to variation in manufacturing process
- *Statistical method from the viewpoint of quality control.* (Shewhart, Deming) 1939, ISBN 0-486-65232-7

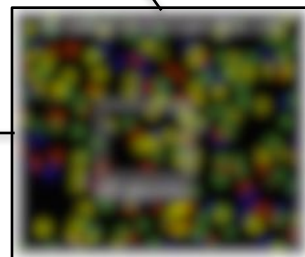
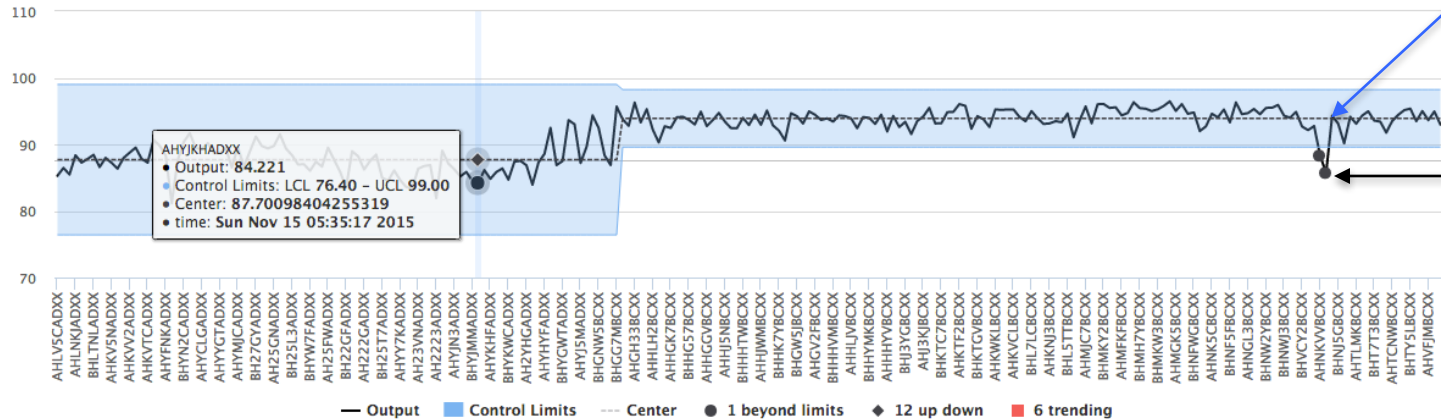
2. Concepts:

- Identify key performance measurements for manufacturing process
- Define statistical transformations to detect variation in process performance
- Chart statistics over time
- Identify common and special causes of variation in manufacturing processes

Q30 Range R1 R3



Q30 Avg R1 R3



Sample CHART_X_BAR_R_R Chart

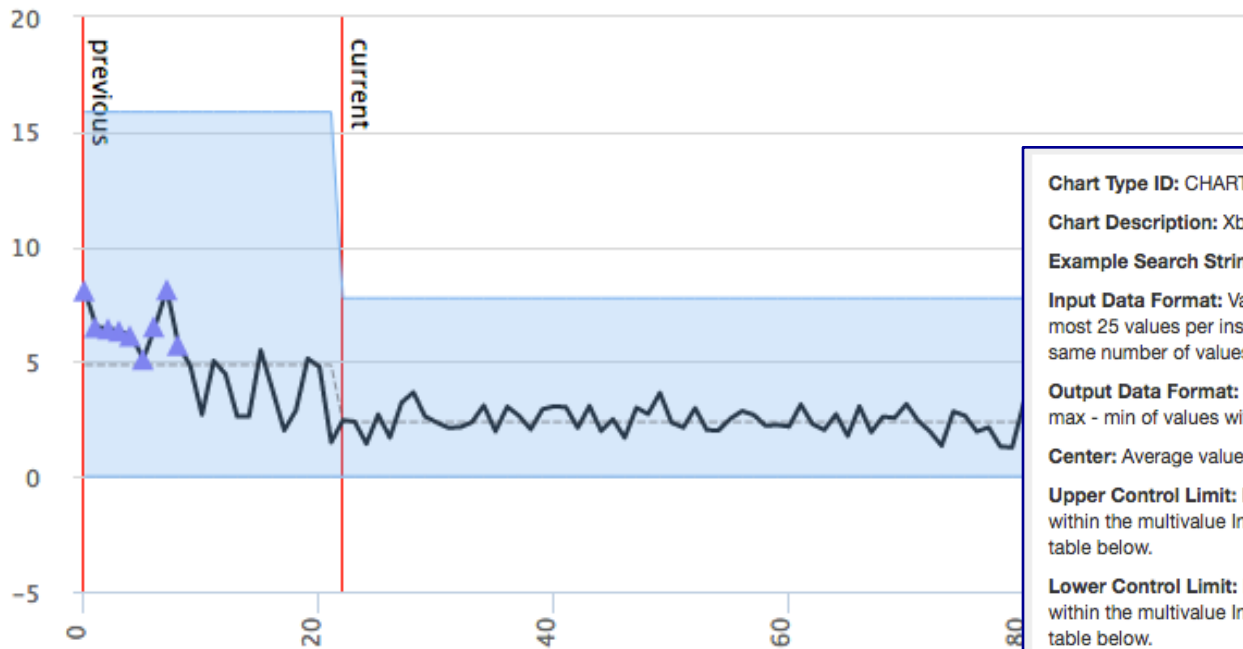


Chart Type ID: CHART_X_BAR_R_R

Chart Description: Xbar R - R

Example Search String: | spc input="Value" charttype=CHART_X_BAR_R_R rules=""

Input Data Format: Value is a multivalue numeric field containing at least two and at most 25 values per instance of the field. All events must contain the field and have the same number of values per field.

Output Data Format: Single value field containing the range from each event. Range = max - min of values within multivalue field.

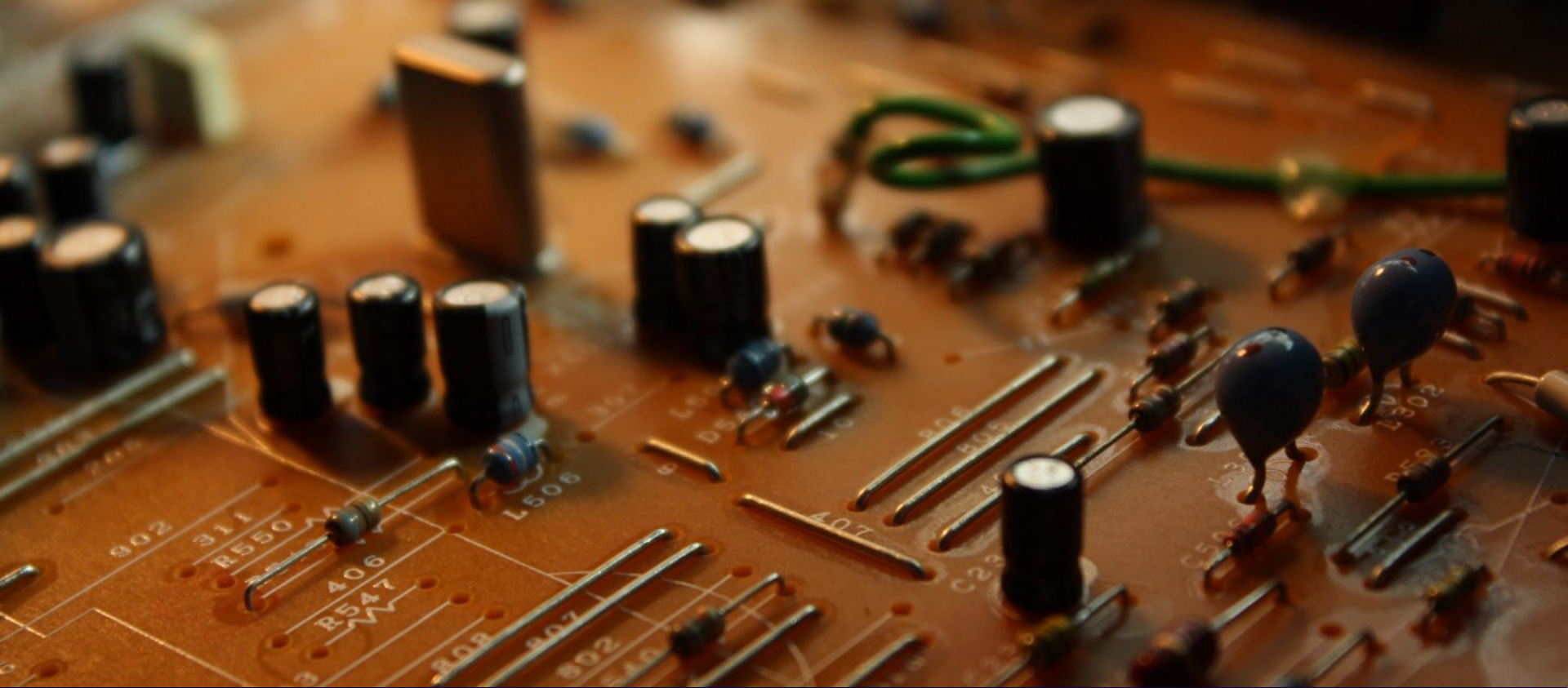
Center: Average value of Output

Upper Control Limit: $D4[n] * \text{Center}$, where n is the number of values for each event within the multivalue Input field, and D4 is an array of control factors described in the table below.

Lower Control Limit: $D3[n] * \text{Center}$, where n is the number of values for each event within the multivalue Input field, and D3 is an array of control factors described in the table below.

Details: Also referred to as an "R Chart" and generally implemented along with a "X-bar Chart" (CHART_X_BAR_R_X).

Tackling Technical Problems



Control Chart Explorer

| inputlookup "rules_sample_data.csv" | where Rule_Set="RULES_1_BEYOND_LIMITS"| Last 24 hours 🔍

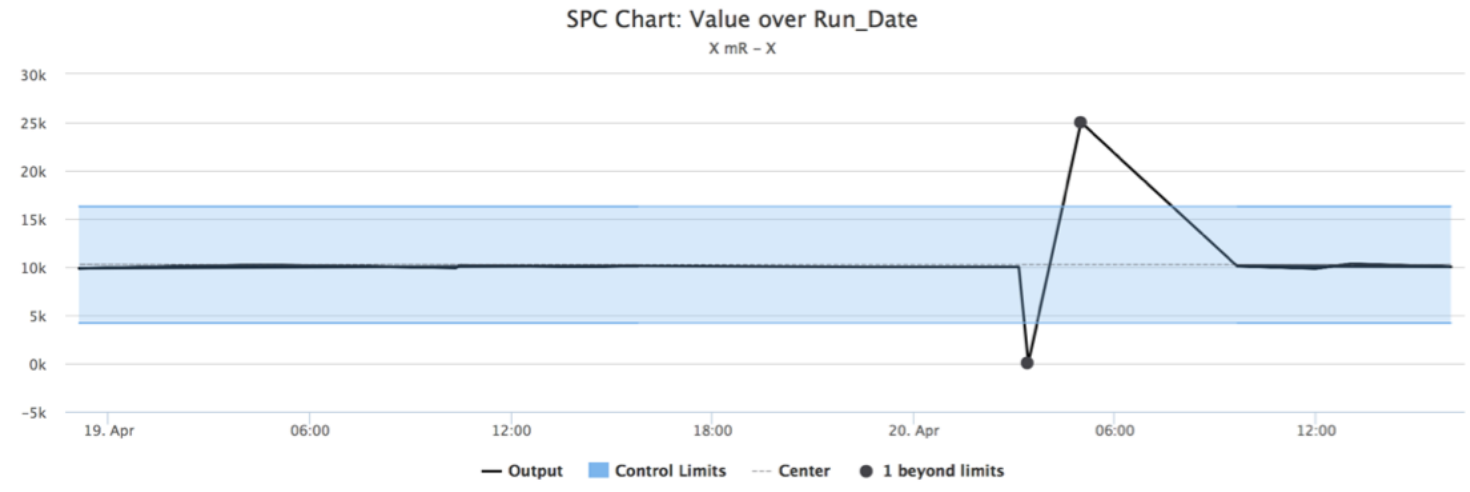
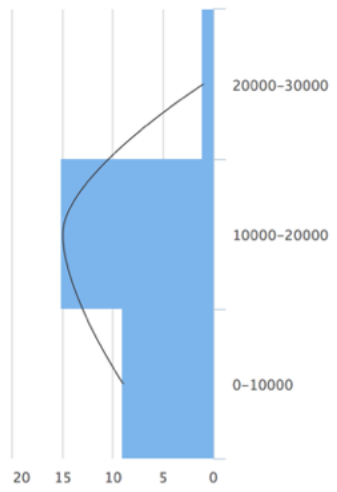
✓ 25 results (8/23/16 8:00:00.000 AM to 8/24/16 8:23:12.000 AM)

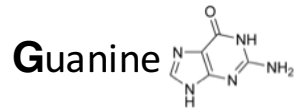
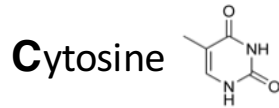
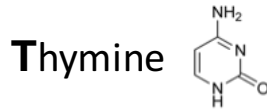
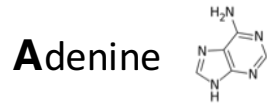
Job ▾ || ■ Smart Mode ▾

Y: X: Chart Type: Tail #: Histogram Buckets:

Extra tooltips: X type: Group by (periods): Rules: Sort:

Name: App:





Automatic Lookups



Teach users to fish



Custom commands



Graphics



Exploratory Dashboards



System/Process Health



Support



Metric Identification



Linking events together

Lessons Learned



Get involved in projects early



Let users shine



Only develop custom code when necessary



Make your UI easy for users



Clear documentation

What's next for Splunk at Myriad?



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Distributed Splunk Infrastructure

- High Availability
- Performance
- Remote offices

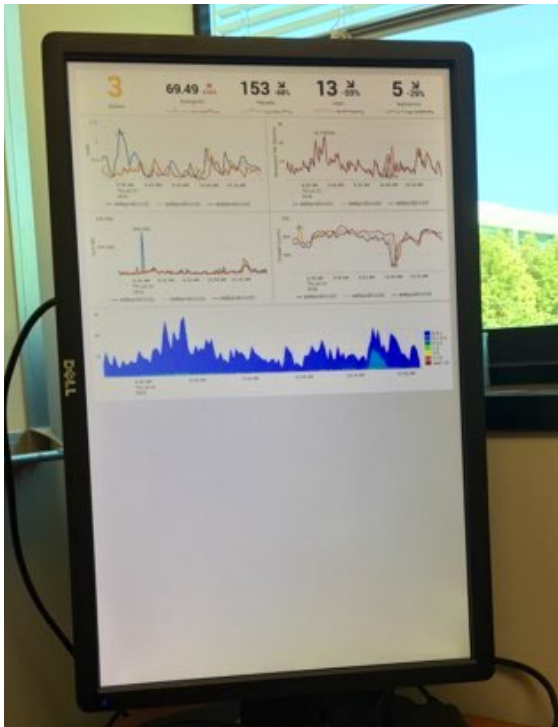


Machine Learning

- Root Cause Analysis
- Preventative Maintenance



Information Radiators



SPLUNK ALL THE THINGS!



Questions?



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THANK YOU

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