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Statistical system to quantify biomolecular samples

Researchers in Prof. Julia Salzman's laboratory have developed an efficient statistically driven tool to improve the accuracy of biomolecules in samples that have a wide range of concentrations. Currently, when nucleic acid samples have both high and low abundance genes (i.e., a large dynamic range), significant resources are necessary to achieve the sequencing depth necessary to reconstruct the original pool using simple random sampling. Conventional processes require designing many sequence-specific steps followed by complicated protocols to reduce the number of abundant species.

Integration of statistics and library preparation drives a sampling approach that uses barcoding and remodels probability distributions to measure biomolecule abundance. Statistical estimation of barcodes are obtained with a novel set of statistical algorithms that decode the signal and reconstruct the initial molecular abundance. This technology uses statistical approaches to increase the information content of the sequenced signal and could also increase precision. Its end user applications include most sequencing applications.

Stage of Research
The inventors have demonstrated proof-of-concept with simulations and experiments.
Simulations:
This method enabled the precise detection of rare species with 10000 sequencing reads compared to 300,000 sequencing reads with conventional statistical sampling techniques.
Experiments:
Using a pool of ~4000 engineered oligonucleotides, the total measured, this method determined the expression level of target sequences with 10 fold fewer sequencing reads than needed for conventional methods.

Applications

- **Nucleic acid quantification** - characterize samples that are currently profiled by next-generation sequencing or qPCR, with end user applications such as:
    - screening of biomolecules
    - in vitro selection with barcodes (molecular selection, aptamer optimization)

Advantages

- **Efficient workflow:**
    - increases statistical inferential power
- **Sensitive:**
    - increased precision to measure molecular abundance
    - improves signal:noise ratio
    - determines absolute numbers of molecules for detected species (compared to random sampling approaches that determine relative concentration)

Patents

- Published Application: WO2019200341
- Published Application: 20210095332
- Issued: 11,466,313 (USA)

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