# Repeatability in Ferrite Nanoparticle Synthesis

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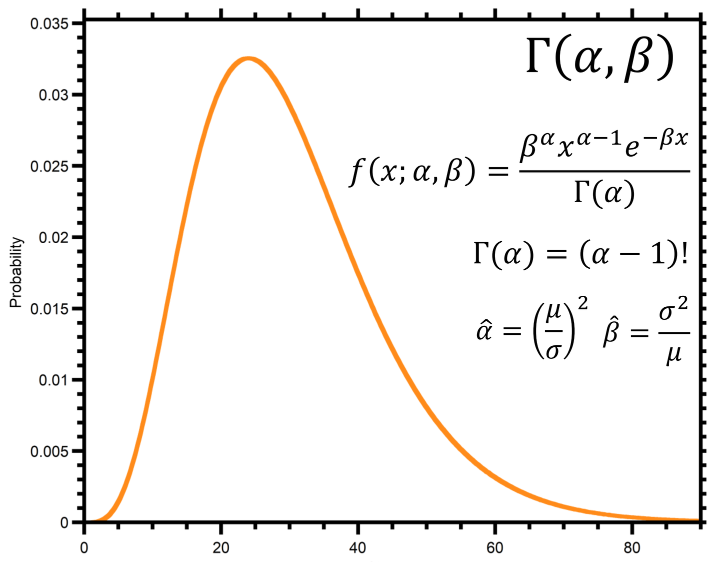
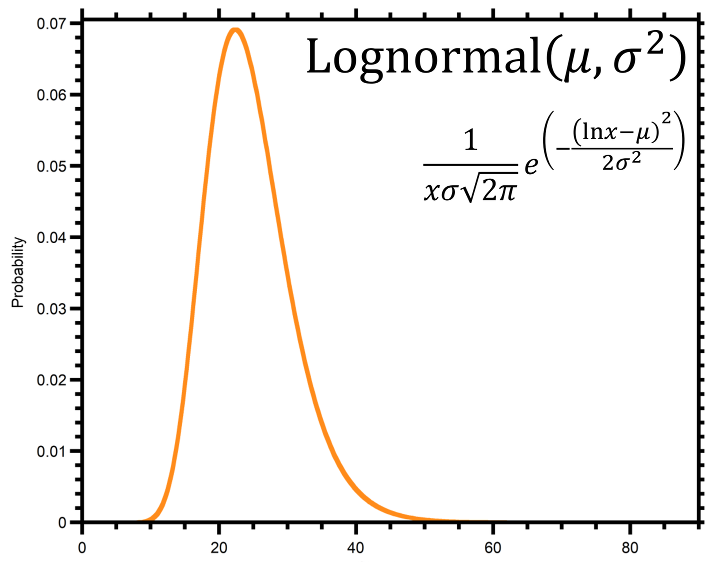
## Introduction

Superparamagnetic nanoparticles – magnetic nanoparticles in which there is a single magnetic domain for the entire particle – have emerging applications in medical theranostics,[1] and high efficiency electronics.[2,3] Since the early 2000s the standard synthesis of superparamagnetic nanoparticles has been a two-step process involving isolation of badly characterized intermediates followed by prolonged heating in high boiling solvent.[4,5] These procedures often suffer from batch-to-batch size inconsistency. Because magnetic properties of interest scale exponentially with particle volume, fine control of size and predictable reaction outcomes are necessary to fully realize the potential of superparamagnetic nanomaterials. Here we present our recent effort toward improving reproducibility in ferrite nanoparticle synthesis. We have developed a convenient, single vessel procedure that gives low dispersity particles of a consistent size. We have benchmarked our procedure against standard methods to demonstrate its superiority.

## Nanoparticles & Their Distributions

Nanoparticle size distributions are often modeled as either Gamma (left) or Log-Normal (right) distributions.




Summing these distributions is mathematically challenging,[6,7] meaning determination of the universal particle distribution for a set of synthetic conditions by repeating the reaction and gathering empirical data is often impractical for the bench chemist needing to evaluate reaction performance.

### Figures of Merit

Pooled Standard Deviation[8]

$$s_{pool} = \sqrt{\frac{s_1^2 + s_2^2 + \cdots + s_k^2}{k}}$$

Coefficient of Variation

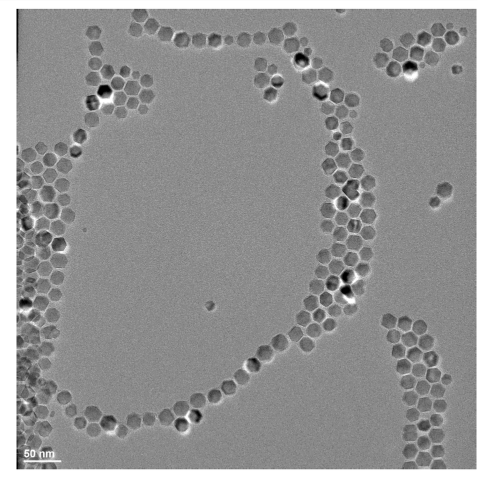
$$CV = \frac{\sqrt{\frac{1}{k}\sum(x_i-\mu)^2}}{\mu}$$

Pooled standard deviation can be calculated as the square root of the average variance from $k$ repeated reactions and gives an estimate of the likely particle distribution width when a reaction is repeated. The coefficient of variation gives an estimate of how far a reaction's mean size will be from the most likely size, $\mu$, the average of observed sizes.

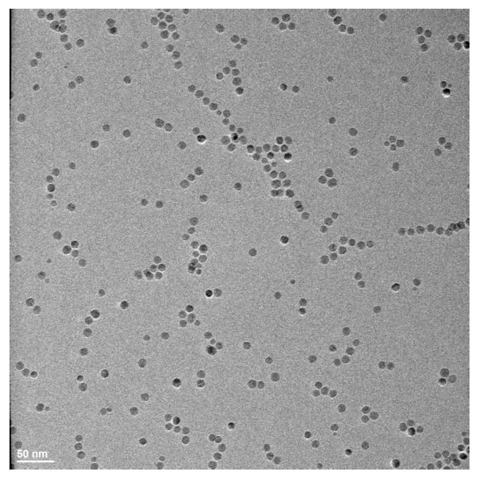
## Literature Procedure Reproducibility

### Krishnan Procedure[5]

| Replicate | Size (nm) [σ, RSD] |
|---|---|
| 1 | 20.01 [1.96, 9.8%] |
| 2 | 22.58 [3.52, 15.6%] |
| 3 | 31.75 [5.87, 18.5%] |
| 4 | 33.07 [5.49, 16.6%] |
| 5 | 29.13 [4.57, 15.7%] |
| Average [$s_{pool}$] | 27.31 [4.51, 16.5%] |



### Hyeon Procedure[4]

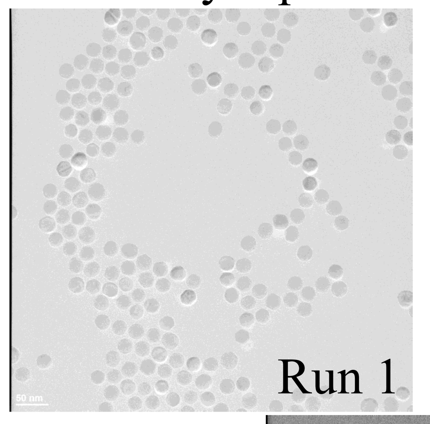


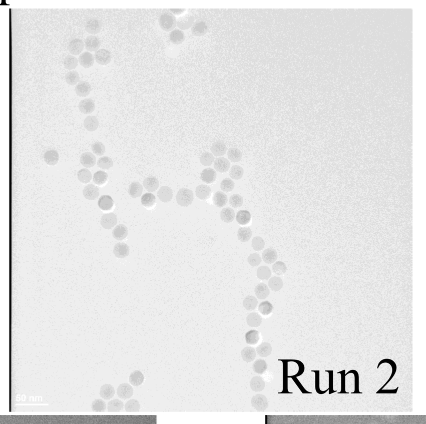
| Replicate | Size (nm) [σ, RSD] |
|---|---|
| 1 | 10.71 [1.16, 10.8%] |
| 2 | 7.63 [0.66, 8.7%] |
| 3 | 6.93 [0.85, 12.2%] |
| 4 | 6.15 [0.67, 10.9%] |
| 5 | 7.06 [1.06, 15.0%] |
| Average [$s_{pool}$] | 7.70 [0.90, 11.7%] |

Examples of two commonly used $Fe_3O_4$ nanoparticle synthesis procedures were evaluated for their reproducibility. Each procedure was repeated five times, and the resulting nanoparticles were evaluated by Transmission Electron Microscopy (TEM) and Small Angle X-Ray Scattering (SAXS). Sizes were determined by SAXS measurements on crude reaction samples. Both procedures rely on synthesis and isolation of poorly characterized Fe-oleate intermediates. The average is the mean of size from the repetitions, with the $s_{pool}$, and $s_{pool}/\mu$ in brackets.

## New Consistent Methodology

In order to develop an $Fe_3O_4$ synthesis with consistent size performance over repeated execution, we pursued a simple one pot procedure. Rather than synthesize and isolate Fe-oleate precursors we generated Fe-oleate species *in situ* using oleic acid as the only solvent. This allowed for substantially higher reaction temperatures, which in turn gave more favorable nucleation dynamics, leading to extremely reproducible particle sizes and distributions.


Run 1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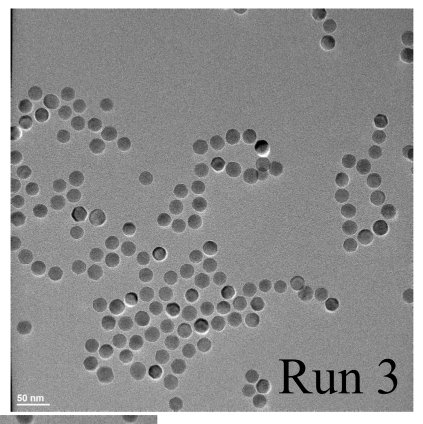
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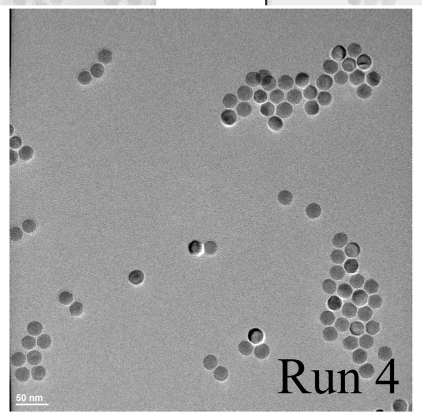
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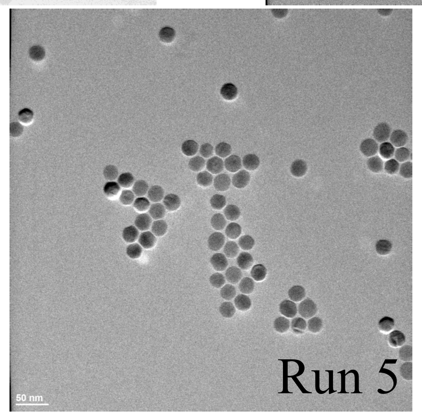

Run 5

| Replicate | One Pot (nm) [σ, RSD] |
|---|---|
| 1 | 23.52 [1.51, 6.4%] |
| 2 | 24.15 [1.74, 7.2%] |
| 3 | 22.34 [1.45, 6.5%] |
| 4 | 22.89 [1.42, 6.2%] |
| 5 | 24.43 [1.76, 7.2%] |
| Avg. [$s_{pool}$] | 23.47 [1.58, 6.7%] |

| Summary | Avg | $s_{pool}$ | CV |
|---|---|---|---|
| One Pot | 23.47 nm | 1.58 nm 6.7% | 3.7% |
| Krishnan | 27.31 nm | 4.51 nm 16.5% | 21.0% |
| Hyeon | 7.70 nm | 0.90 nm 11.7% | 22.9% |

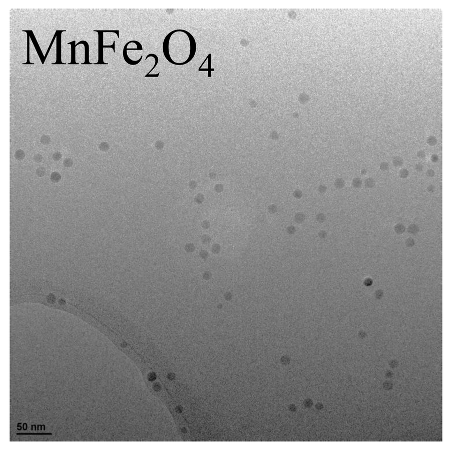
## Conclusions & Future Directions

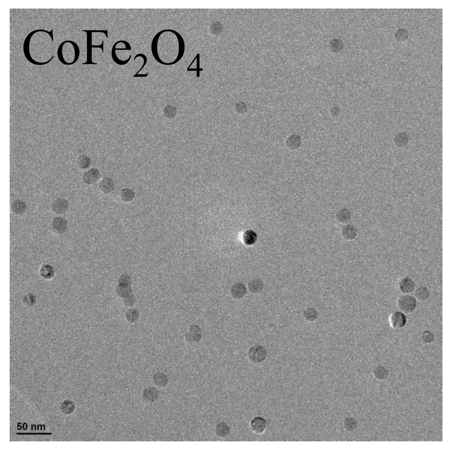
### Conclusion

In an effort to improve synthetic predictability in $Fe_3O_4$ NP forming reactions we have developed a simple, one pot procedure that gives low dispersity products with a predictable size. In addition, owing to the mathematical complication of summing distributions, we have borrowed easy to calculate figures of merit from the field of error analysis in the form if $s_{pool}$ and CV. Our new one pot procedure significantly out performs standard literature methods for the preparation of superparamagnetic magnetite NPs.

### Future Directions

Magnetite nanoparticles are not the only superparamagnetic materials of interest. In addition to size, nanomaterial magnetic properties can be modified by changing nanoparticle composition. We are presently developing reproducible methodology.

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