Using shooting approaches to generate initial guesses for ODE parameter estimation

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August 19, 2019

Outline

Parameter Estimation for ODEs

Shooting Approaches

Generating Initial Guesses

Proposed Methods

Numerical Example

ODEs

We consider the initial value problem (IVP),

$$\dot{\boldsymbol{y}}(t) = \boldsymbol{f}(t, \boldsymbol{y}(t), \boldsymbol{p})$$
$$\boldsymbol{y}(0) = \boldsymbol{y}_0$$
$$t \in [0, T]$$

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- Numerous numerical methods exist for approximating $\boldsymbol{y}(t, p)$ that satisfy this IVP
- Most methods simulate the **trajectory**, $\boldsymbol{y}(t, p)$, starting from $\boldsymbol{y}(0)$. (e.g. continuous Runge-Kutta with defect control Enright and Yan (2010))

Parameter Estimation

- The goal of parameter estimation is to estimate the parameters, $\hat{\boldsymbol{p}}$, that make the model best fit the observed data $(\hat{\boldsymbol{y}}(t_i) = \boldsymbol{y}(t_i) + N(0, \sigma^2),\ i = 1, \ldots, n_o\ )$.

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- This is a non-linear least squares problem.

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\hat{\boldsymbol{p}} &= \arg\min_{\boldsymbol{p}} \sum_{i=1}^{n_o} \frac{\|\hat{\boldsymbol{y}}(t_i) - \boldsymbol{y}(t_i, \boldsymbol{p})\|^2}{2\sigma^2} \\
&= \arg\min_{\boldsymbol{p}} L(\boldsymbol{p})
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We will consider using **shooting approaches** - Given $\boldsymbol{p}$, simulate the ODE IVP to approximate $y(t, \boldsymbol{p})$ whenever evaluating $L(\boldsymbol{p})$.

Shooting Approaches

Simple (or single) shooting (e.g. Bard (1974))

- Choose an initial guess, $\boldsymbol{p}_o$

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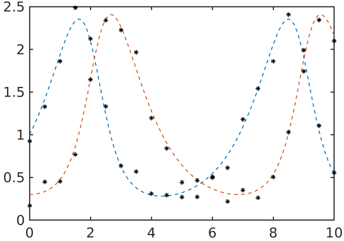
- simulation may fail for some values of $\boldsymbol{p}$ before time T

If $\boldsymbol{p}_o$ is close enough to $\hat{\boldsymbol{p}}$, single shooting typically works quite well.

Example: Barnes Problem

Lotka-Volterra Predator-Prey Model



- oscillatory trajectory
- global minimum sometimes found with single shooting.

$$y_1'(t) = p_1 y_1(t) - p_2 y_1(t) y_t(2)$$
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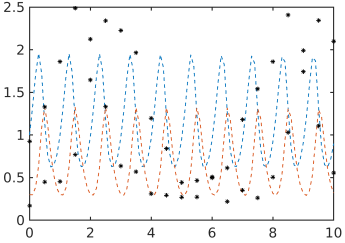

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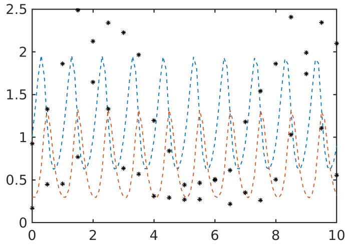

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Insight: Once the trajectory begins to diverge, how well it fits the rest of the data isn't really useful.

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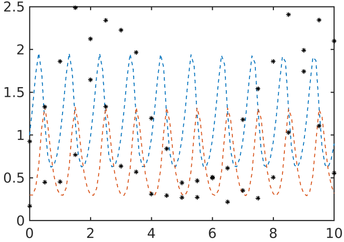

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Idea: Only fit to the first part of the data initially.

More Robust Shooting Approaches

Incremental (or progressive) shooting (Michalik et al., 2009; Krogh et al., 1985)

- simulate the ODE IVP to approximate $y(t, \boldsymbol{p})$ from $t = 0$ up to s ($s \leq T$).

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- Set $\boldsymbol{p}_o = \hat{\boldsymbol{p}}(s)$.
- Increment s and repeat until $s = T$. ($\hat{\boldsymbol{p}}(T) = \hat{\boldsymbol{p}}$)

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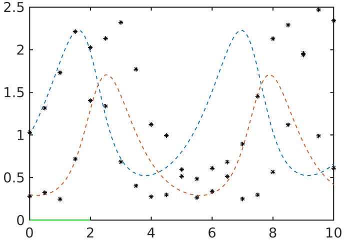

Initially $s = 2$, we increment by 2

- Incremental shooting can succeed here - less sensitive to $\boldsymbol{p}_o$.

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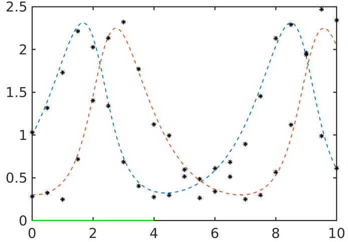

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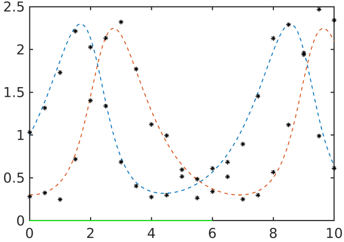

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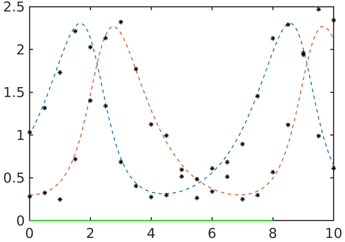

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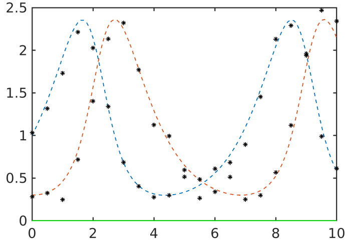

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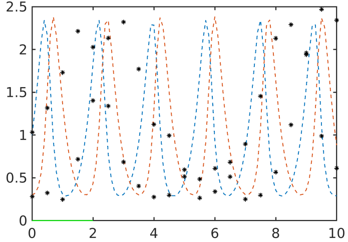

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- Poor local minimum still sometimes found with incremental shooting.

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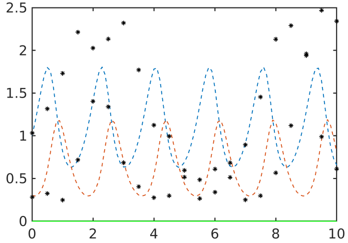

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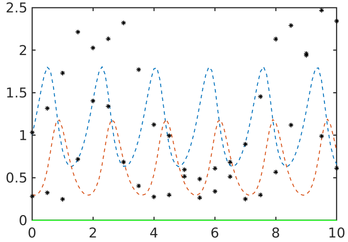

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Insight: It might help to use all of the observations

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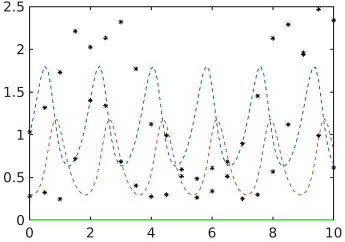

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Idea: reset the trajectory and keep simulating

More Robust Shooting Approaches

Multiple shooting (Bock and Plitt, 1984; Peifer and Timmer, 2007)

- Split the interval $[0, T]$ into n_{MS} sub-intervals (i.e. generate a mesh, $\{0 = \tau_0, \tau_1, \ldots, \tau_{n_{MS}} = T\}$)

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- Add an equality constraint at each sub-interval boundary $y(\tau_i)^- = y(\tau_i)^+$
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Can initialize each $y(\tau_i)^+$ using nearby observed data points

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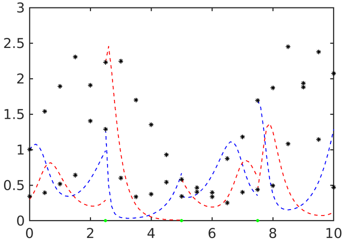

We used $n_{MS} = 4$, uniform spacing

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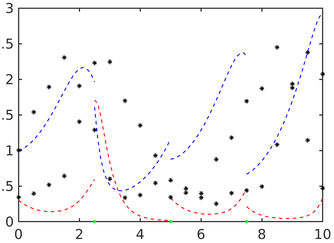

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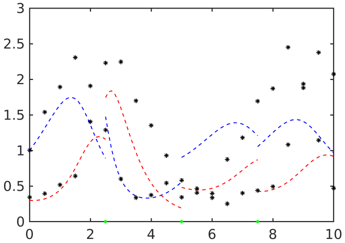

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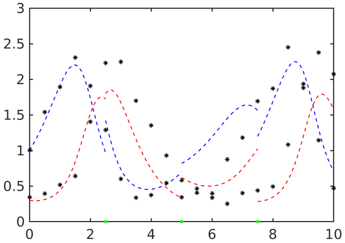

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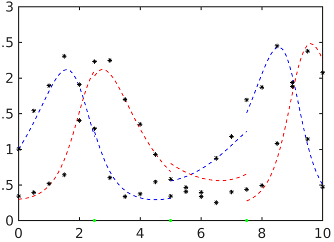

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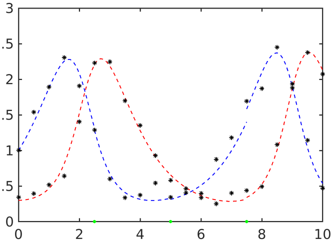

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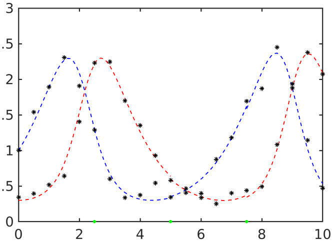

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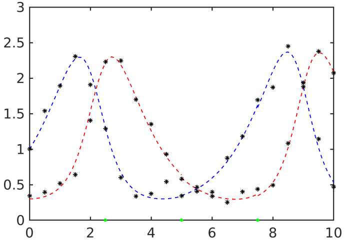

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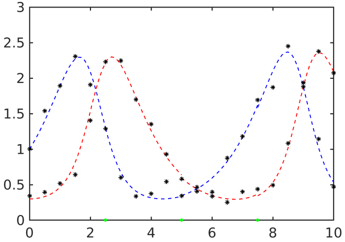

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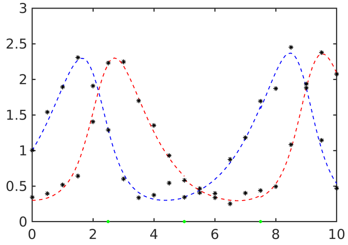

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Try 100 random samples for $\boldsymbol{p}_o$ from $[0, 10]^3$

	simple	incremental	multiple
convergence	5%	39 %	48 %
median time	0.1s	0.36s	0.15s

Methods for obtaining a suitable $\boldsymbol{p}_o$

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- $\tilde{\boldsymbol{y}}$ is obtained by smoothing the observations

Integral smooth and match (INT-SME)

- Gugushvili et al. (2012) proposed using the integral form of the ODE IVP instead.

$$\min_{\boldsymbol{y}_0,\boldsymbol{p}} \int_0^T \left\| \tilde{y}(t) - \left(\boldsymbol{y}_0 + \int_0^t f(s, \tilde{y}(s), \boldsymbol{p})\, ds\right) \right\|^2 dt,$$

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This is the method we will consider for the rest of this talk

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- Similar approach to DBE that uses the integral form also recently appeared in the UQ literature (Green and Rindler, 2019)

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Case of Linear Parameters

- Sometimes the parameters appear linearly in $f(t, \boldsymbol{y}(t), \boldsymbol{p})$.
- $\boldsymbol{p} = \boldsymbol{r}$

$$f(t, \boldsymbol{y}(t), \boldsymbol{p}) = G(t, \boldsymbol{y}(t))\boldsymbol{r}$$

- INT-SME becomes:

$$\arg\min_{\boldsymbol{r}, \boldsymbol{y}_0} \int_0^T \left\| \tilde{\boldsymbol{y}}(t) - (\boldsymbol{y}_0 + [\int_0^t G(s, \tilde{\boldsymbol{y}}(s))\, ds]\, \boldsymbol{r}) \right\|^2 dt.$$

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INT-SME is a linear least squares problem

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- INT-SME becomes:

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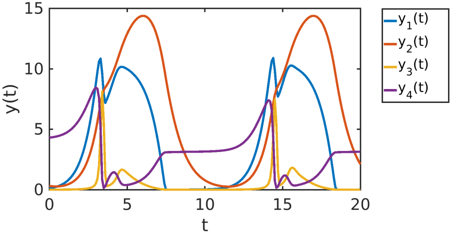
For a given $\tilde{\boldsymbol{y}}(t)$, this gives only one candidate $\boldsymbol{p}_o$

Calcium Ion Test Problem [Kummer et al. (2000) Peifer and Timmer (2007)]

$$G^*{}_\alpha{}' = k_1 + k_2 G^*{}_\alpha - k_3 PLC^* \frac{G^*{}_\alpha}{G^*{}_\alpha + Km_1} - k_4 Ca_{cyt} \frac{G^*{}_\alpha}{G^*{}_\alpha + Km_2},$$
$$PLC^{*\prime} = k_5 G^*{}_\alpha - k_6 \frac{PLC^*}{PLC^* + Km_3},$$
$$Ca_{cyt}{}' = k_7 PLC^* Ca_{cyt} \frac{Ca_{er}}{Ca_{er} + Km_4} + k_8 PLC^* + k_9 G^*{}_\alpha - k_{10} \frac{Ca_{cyt}}{Ca_{cyt} + Km_5} - k_{11} \frac{Ca_{cyt}}{Ca_{cyt} + Km_6},$$
$$Ca_{er}{}' = -k_7 PLC^* Ca_{cyt} \frac{Ca_{er}}{Ca_{er} + Km_4} + k_{11} \frac{Ca_{cyt}}{Ca_{cyt} + Km_6},$$

- 11 linear parameters (k) to be estimated
- 6 non-linear parameters (Km) [held fixed]
- 6.5% relative noise added to true trajectory sampled at 200 uniformly spaced times
- initial conditions assumed known



Calcium Ion Test Problem Results

method	converged	avg time of converged (s)
SS	4 %	44 ± 16
MS	49 %	48 ± 58

Table: Results reported in Peifer and Timmer (2007). The trajectory simulations were performed using ODESSA and a Gauss-Newton optimizer. They generated one set of noisy data and ran each of simple shooting (SS) and multiple shooting (MS) with $n_{MS} = 17$ from 250 random initial guesses for $\boldsymbol{p}_o$, which were drawn uniformly from $[0, 1]^{11}$.

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- 63% success rate if we use INT-SME to generate $\boldsymbol{p}_o$ and then use simple shooting.
- time: $1.1s \pm 2.2s$

Proposed Methods
Motivation

Why does INT-SME sometimes fail?
The integrals,

$$\int_0^t G(s, \tilde{\boldsymbol{y}}(s))\, ds,$$

may accumulate errors.

- only use a subset of the data? (like progressive shooting)

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We consider the first two ideas here.

Proposed Methods

First, we define INT-SME(s):

$$\min_{\boldsymbol{r}} \int_0^{s} \left\| \tilde{\boldsymbol{y}}(t) - (\boldsymbol{y}_0 + [\, \int_0^t G(\tau, \tilde{\boldsymbol{y}}(\tau))\, d\tau]\, \boldsymbol{r}) \right\|^2 dt,$$

where $0 < s \leq T$.

Incremental Shooting - only consider data up to time s.

Proposed Methods

INT-SME(m,s)

$$\sum_{i=1}^{m} \left[\int_{t_i}^{t_{i+1}} \left\| \tilde{y}(t) - \left(y(t_i)^{+} + \left[\int_{t_i}^{t} G(\tau, \tilde{\boldsymbol{y}}(\tau))\, d\tau \right] r \right) \right\|^2 dt \right],$$

- m is the number of intervals used

Proposed Methods

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- m is the number of intervals used
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- m is the number of intervals used
- the set of t_i's partition the interval from 0 to s.
- In our numerical experiments, we use uniform partitions.
- Unlike true multiple shooting, we do not enforce equality constraints at the end of each shooting interval.

Proposed Methods

Let $S = \{s_1, s_2, \ldots s_{N_{PS}}\}$.

INT-SME(S):

$$\min_{\boldsymbol{p} \in P_o} L(\boldsymbol{p}),$$

where the i'th element in P_o, is $\boldsymbol{p}_i = \text{INT-SME}(s_i)$

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Calcium Ion Results

m \ s	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
1	96	98	98	92	93	85	95	92	94	95	92	84	72	66	65	63
2	93	100	92	90	98	98	98	100	95	95	98	91	80	66	55	64
4	98	100	98	92	97	100	100	99	98	97	98	96	94	93	86	91
8	98	100	99	100	100	100	99	99	100	100	100	99	98	99	98	100
16	99	100	100	98	100	100	100	100	100	100	100	100	100	100	99	100
PS	96	97	100	98	100	100	100	99	100	100	100	100	100	100	100	100

Table: What percentage of times the final optimization succeeded when INT-SME(m,s) was used to generate $\boldsymbol{p}_o$ using different values of m and the data up to time s.

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Table: What percentage of times the final optimization succeeded when INT-SME(m,s) was used to generate $\boldsymbol{p}_o$ using different values of m and the data up to time s. The last line, PS, corresponds to using INT-SME(S), with $S = \{5, 6, \ldots, s\}$.

- top row: simple shooting is poor if we use all the data (63%)
- multiple shooting improves as we add more intervals
- bottom row: INT-SME(S) generates more candidates for $\boldsymbol{p}_o$ as we move right in the table

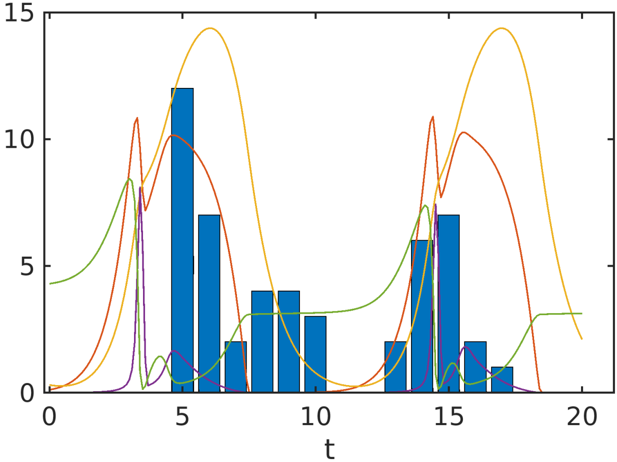
Additional Remarks

m \ s	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
1	0.87	0.84	0.92	0.89	1.00	0.85	0.83	0.98	0.91	0.85	0.86	1.01	1.45	1.48	1.31	1.65
2	0.93	0.84	0.85	0.93	0.91	0.86	0.89	0.93	1.05	0.80	0.93	1.18	1.17	1.55	1.32	1.57
4	0.91	0.77	0.84	0.97	0.80	0.83	0.83	0.89	0.86	0.85	0.93	0.92	1.04	1.08	1.31	1.19
8	0.87	0.81	0.86	0.86	0.81	0.81	0.83	0.81	0.82	0.85	0.85	0.86	0.94	0.98	0.90	0.95
16	0.98	0.92	0.93	0.89	0.90	0.92	0.92	0.95	0.92	0.95	0.91	0.96	0.98	1.04	1.01	1.03
PS	0.94	0.82	0.82	0.79	0.80	0.79	0.83	0.79	0.82	0.76	0.81	0.79	0.79	0.78	0.77	0.78

Table: Time taken for the full procedures.

- in all cases, run time is 0.8s - 1.6s.
- most of this time is for the final optimization.
- PS-INT-SME generates a better $\boldsymbol{p}_o$ as more candidates are considered.

Which INT-SME(s) is PS-INT-SME([5:20]) using for $\boldsymbol{p}_o$?



Histogram of which INT-SME(s) is being used as $\boldsymbol{p}_o$, overlaid with the true trajectory

- The best $\boldsymbol{p}_o$'s don't use all of the data.

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Joint work with Wayne Enright and Jienan Yao

Thanks for Listening

Questions?

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