Syntrophic exchange in synthetic microbial communities

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Background

- cooperation+competition $\longrightarrow$ stability,maintenance and longevity

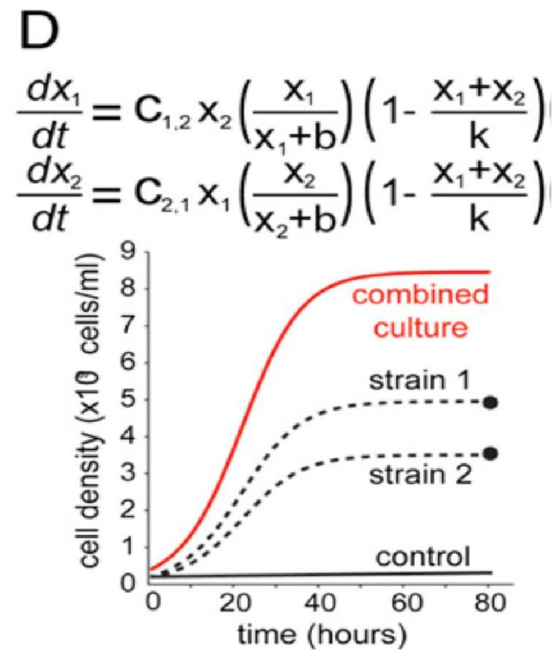- general principle?? (microbial ecology、 engineering synthetic microbiomes)
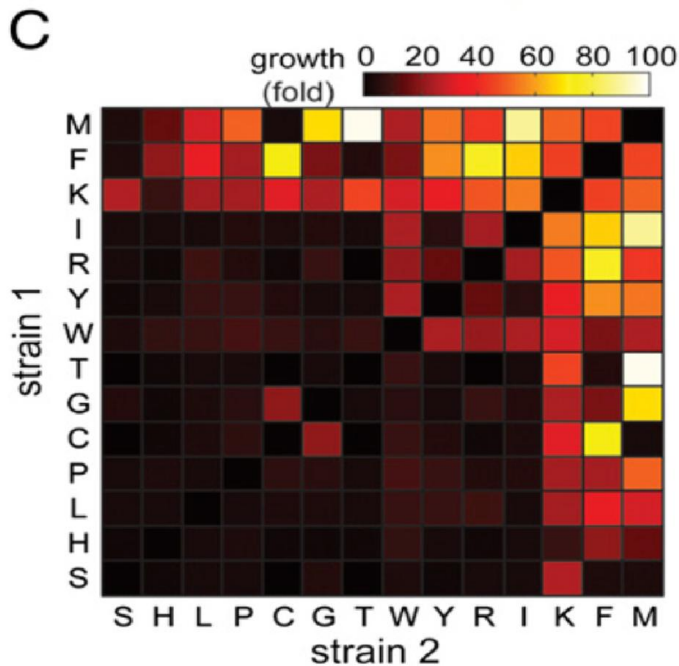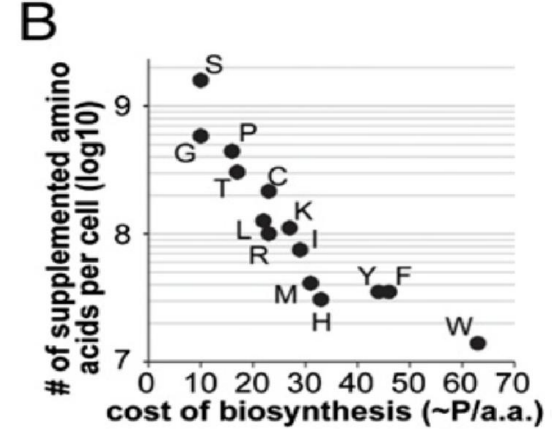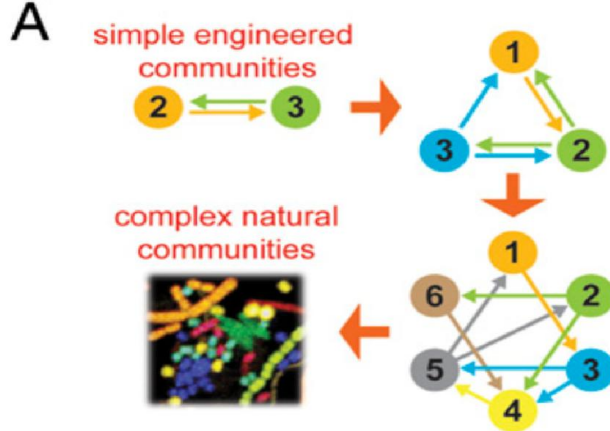
- exchange of essential metabolities(metabolic crossfeeding)

- amino acid exchange $\longrightarrow$ gain new insights into basic principles in metabolic crossfeeding

Procedure

- pairwise syntrophic communities
- three-member synthetic consortia
- 14-member community
- comparative genomic analysis of amino acid biosynthesis

# Pairwise Syntrophic Communities

- 14 mutant strains(auxotrophic phenotype of 1 of 14 essential amino acids)
- grow only when supplemented with each amino acid needed
- 91 possible pairwise syntrophic interactions
- M9-glucose minimal media for 84h

A simple engineered communities

complex natural communities

B

# of supplemented amino acids per cell (log10)

cost of biosynthesis (~P/a.a.)

C

growth (fold) 0 20 40 60 80 100

strain 1

M F K I R Y W T G C P L H S

S H L P C G T W Y R I K F M

strain 2

D

$$\frac{dx_1}{dt} = C_{1,2}\, x_2 \left(\frac{x_1}{x_1+b} \right) \left(1 - \frac{x_1+x_2}{k} \right)$$

$$\frac{dx_2}{dt} = C_{2,1}\, x_1 \left(\frac{x_2}{x_2+b} \right) \left(1 - \frac{x_1+x_2}{k} \right)$$

cell density (x10 cells/ml)

combined culture

strain 1

strain 2

control

time (hours)

Metabolic crossfeeding in syntrophic communities

Three-member Synthetic Consortia

- 91 double-amino acid auxotrophic derivatives
- grow in the presence of extracellular supplementation of both needed amino acid
- 364 possible three-member syntrophic consortia （MF、MK、FK）
- M9-glucose minimal media for 84h
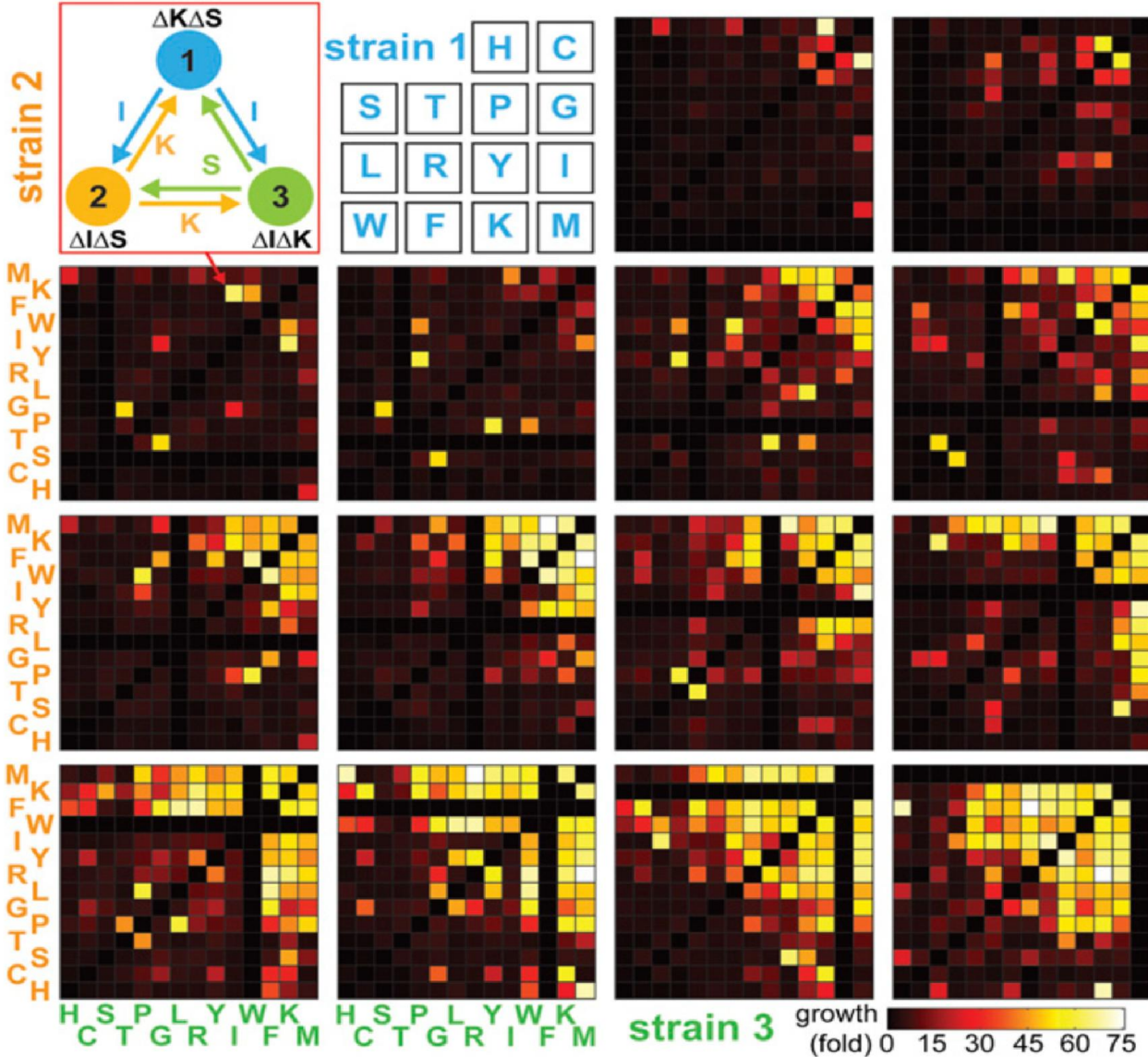
Three-member syntrophic consortia with each strain being auxotrophic for two amino acids
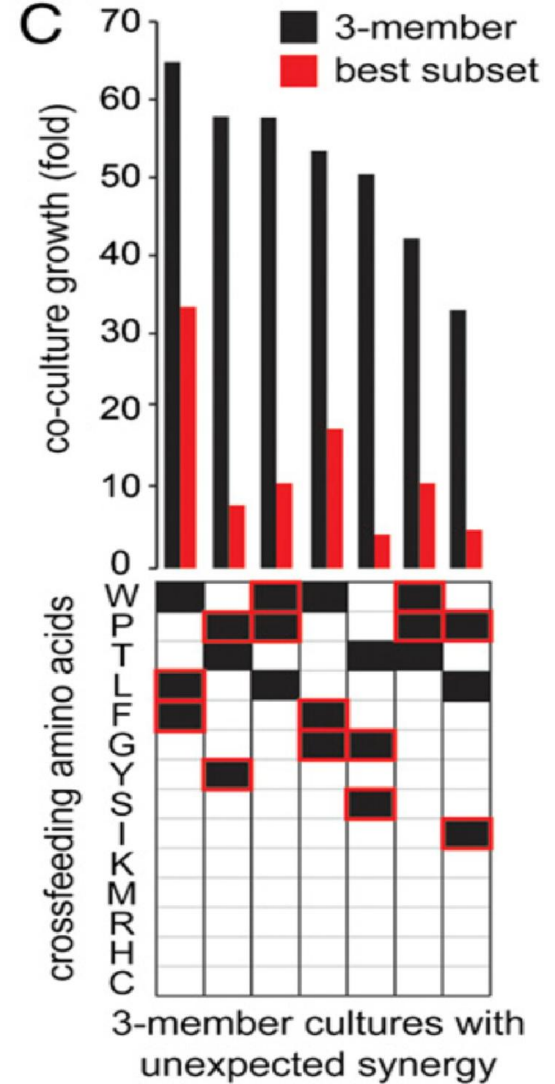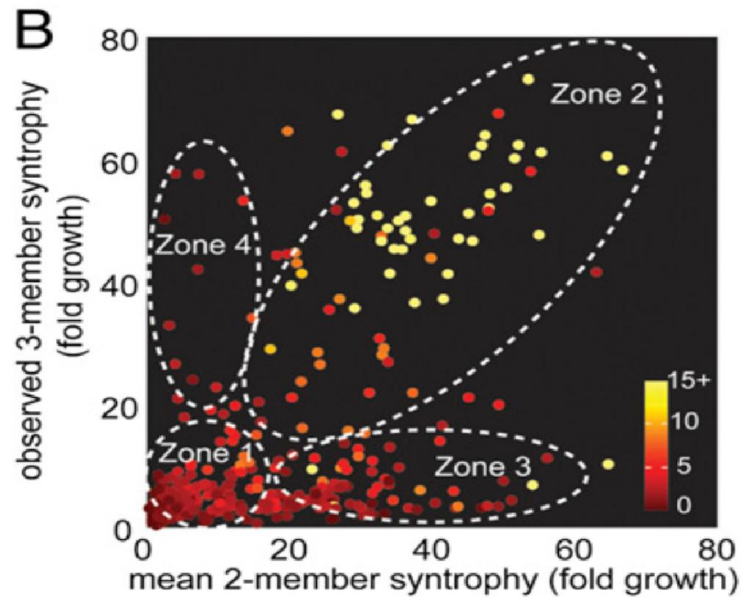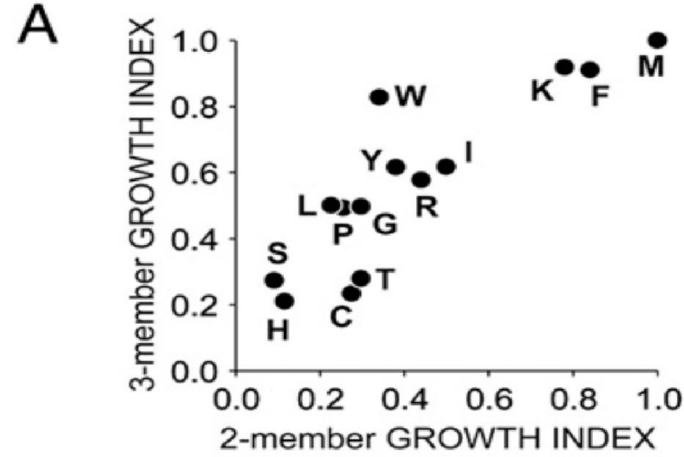
Comparison of three-member syntrophies composed of double auxotrophs against two-member composed of single auxotrophs

- three-member dynamic model

$$\frac{dX_1}{dt} = \frac{X_1}{X_1 + \beta} \cdot \min(c_{1,2}X_2, c_{1,3}X_3) \left(\frac{1 - (X_1 + X_2 + X_3)}{k} \right),$$

$$\frac{dX_2}{dt} = \frac{X_2}{X_2 + \beta} \cdot \min(c_{2,1}X_1, c_{2,3}X_3) \left(\frac{1 - (X_1 + X_2 + X_3)}{k} \right),$$

$$\frac{dX_3}{dt} = \frac{X_3}{X_3 + \beta} \cdot \min(c_{3,1}X_1, c_{3,2}X_2) \left(\frac{1 - (X_1 + X_2 + X_3)}{k} \right),$$

14-member community

- partial syntrophy（MK-HF）to strict syntrophy（MF-MK-HF）
- test the predicted reduction from partial to strict syntrophy by devising a synthetic consortium using the 14 monoauxotrophs
- dynamic model

$$\dot{X_i} = \frac{X_i}{X_i + \beta} \left(\sum_{j=1, j \neq i}^{14} c_{ij} X_j \right) \left(\frac{1 - \sum_{j=1}^{14} X_j}{k} \right)$$

- test 13-member consortia(probe the structure of the syntrophic network)
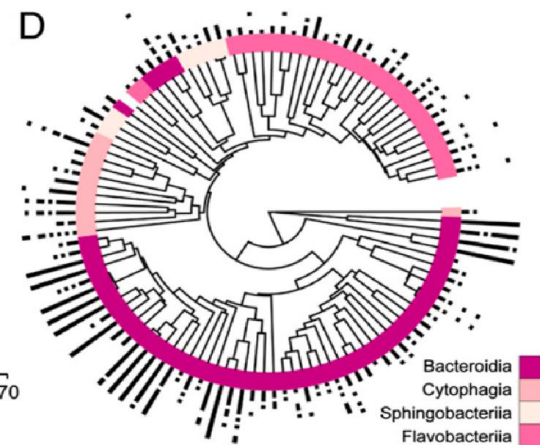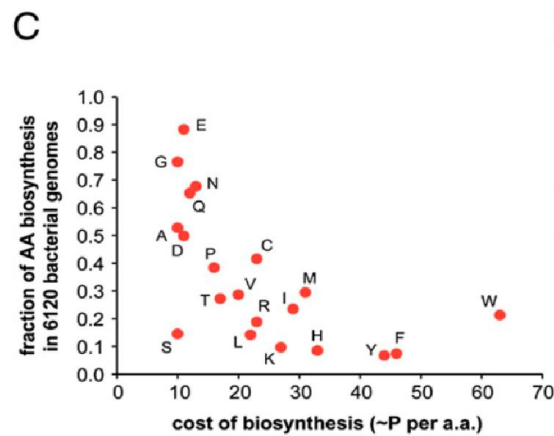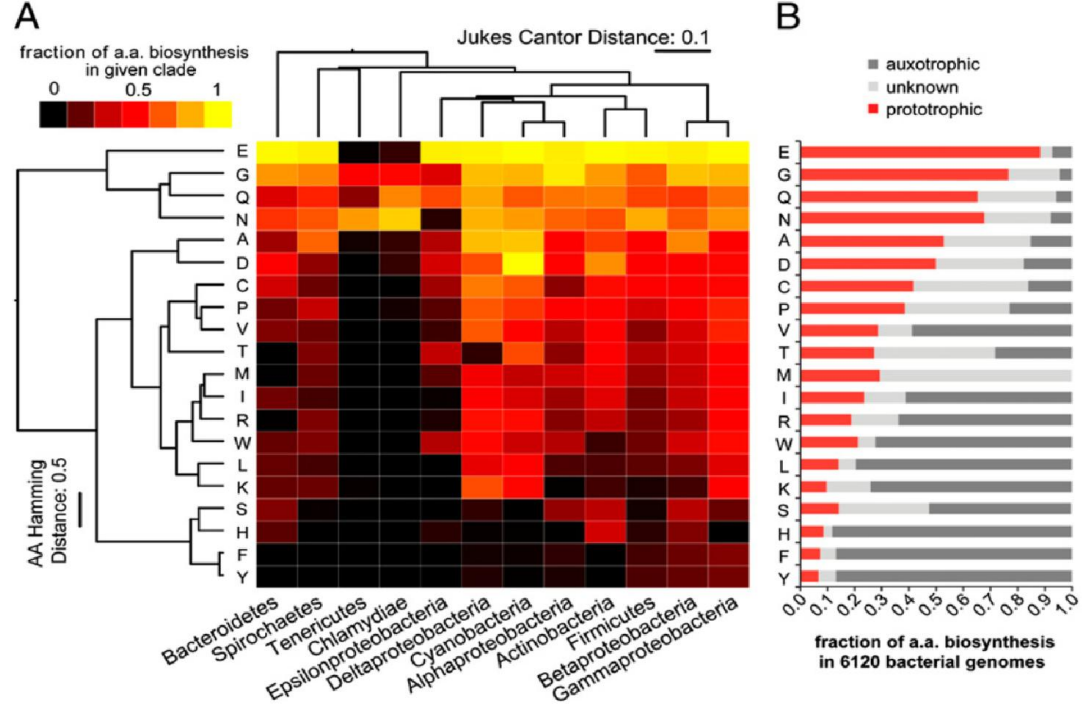- R、K、M、T(dominant strains)
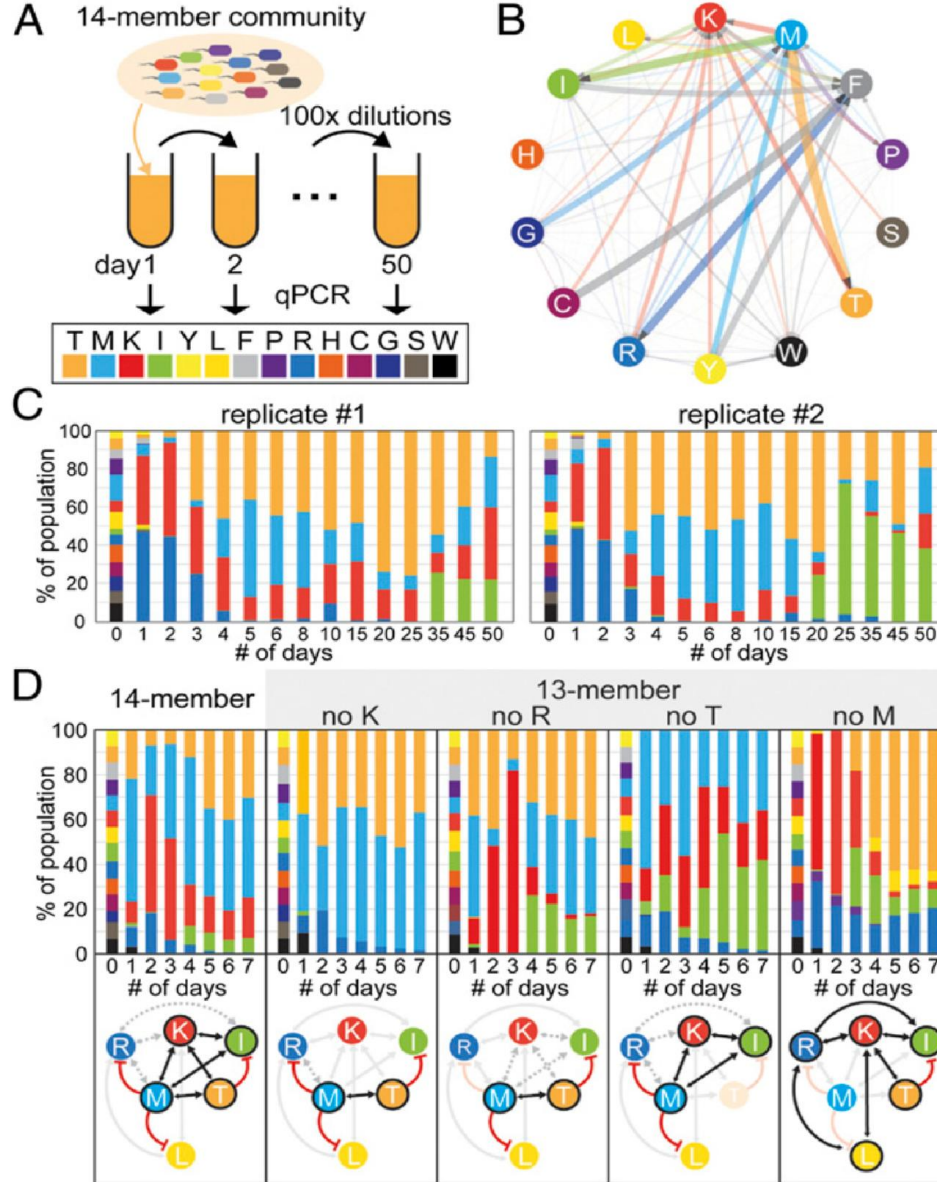
Dynamics of a 14-member syntrophic consortium

Comparative Genomic Analysis Of Amino Acid Biosynthesis

Hypothesize

- Amino acid exchange may be an important property across many microbial communities in the natural biosphere

Amino acid biosynthesis in the microbiome

Summarize

- Flaw:
- 1. It's better for the author to probe the syntrophic interactions of the 12-member consortia and the 11-member consortia besides that of the 13-member consortia.
- 2. It's better for the author to search the exchange of other metablioties containing nucleotides and so on.
- 3. It's better for the author to use other Genus strains to verify the conclusion .

Summarize

- Conclusion: The significant syntrophic interactions is dominated by four amino acid including M、R、K、T.

- Enlightment: The construction of the biological model can not only suggest the principles of the biological interactions but also be verified by the experiments.

Thank You