Omics研究のボトルネックPhenomics：見えるもの、見えないものをどう計るか？

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Phenomicsが拓く遺伝・育種研究
@かずさDNA研究所
2012/03/09 10:45-11:20

次世代シークエンサー(NGS)がもたらしたゲノミックスの新時代

1ランで600 Gb

ヒトゲノム（約30億塩基対）の約200倍、
イネゲノム（約4億塩基対）の約1500倍

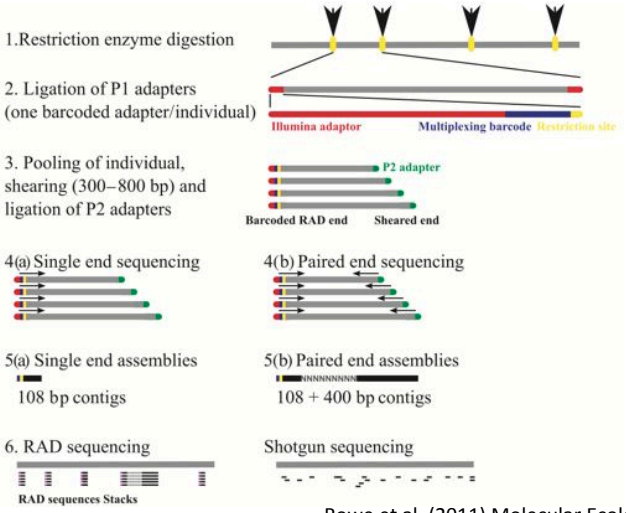
We are now entering another new era in genomics where high throughput sequencing technologies will make re-sequencing of genomes to examine allelic variation affordable and fast, and gene expression analysis by cDNA sequencing will render microarray technologies obsolete. **We will be presented with terabytes of sequence information, both from genomic and transcriptional origin, which will need to be given functional meaning.**

Furbank 2009 Func Plant Biol 36:5

Oxford Nanopore Technologies
USBメモリサイズのシークエンサー

$900で数10 Gb (ヒトゲノム 3Gb)

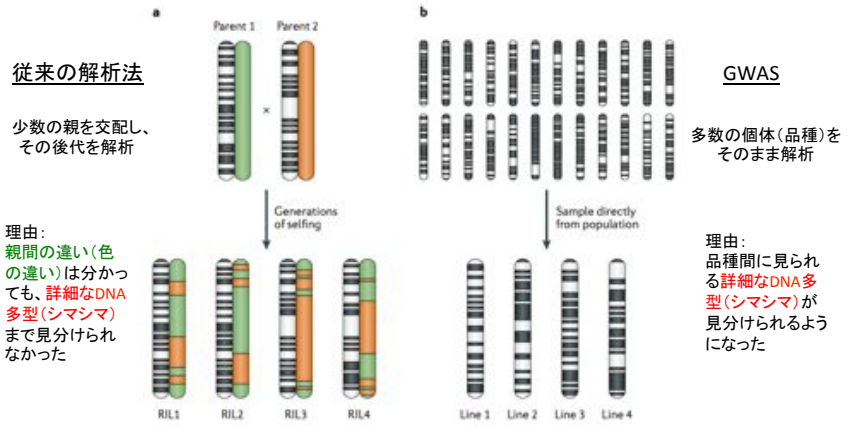
NGSを使った多検体ジェノタイピング
RAD, GBS etc…



Rowe et al. (2011) Molecular Ecology 20:3499

交配実験を行わずに遺伝子検出

（Genome-wide association study: GWAS）



Morrell et al. (2012) Nature Review Genetics 13:85

従来の解析法

少数の親を交配し、その後代を解析

理由：
親間の違い（色の違い）は分かっても、詳細なDNA多型（シマシマ）まで見分けられなかった

解像度が低い、材料作りに時間がかかる

GWAS

多数の個体（品種）をそのまま解析

理由：
品種間に見られる詳細なDNA多型（シマシマ）が見分けられるようになった

解像度が高い、交配を行う必要がない
ただし、従来法より多くのサンプルを要する

従来法 + GWAS = Nested Association Mapping

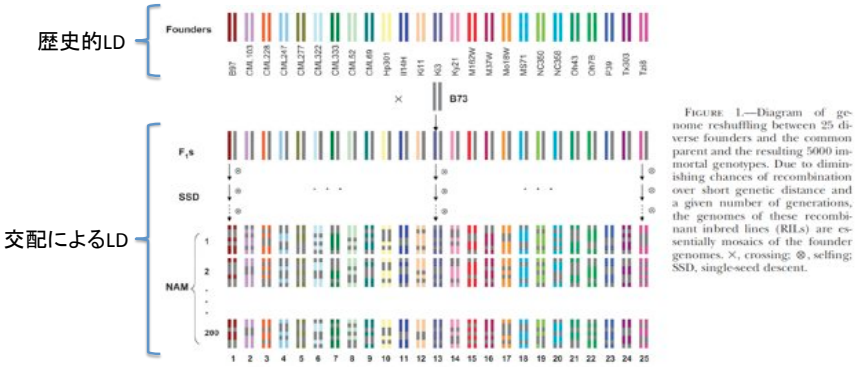


FIGURE 1.—Diagram of genome reshuffling between 25 diverse founders and the common parent and the resulting 5000 immortal genotypes. Due to diminishing chances of recombination over short genetic distance and a given number of generations, the genomes of these recombinant inbred lines (RILs) are essentially mosaics of the founder genomes. ×, crossing; ⊗, selfing; SSD, single-seed descent.

- 歴史的に生じた連鎖不平衡と交配によって生じた連鎖不平衡の両方の情報を利用してQTLを検出する
- GWASと異なり、遺伝的背景の影響を受けにくい
- 多くのサンプルを必要とする

Yu et al. (2008) Genetics 178: 539-551

娘牛がミルクを生産するのを待たずして…

← 24頭のウシの、54,609箇所のDNA多型を、一度に解析できるチップ

NEWS

GOT A NEWS TIP? Send any article ideas for Nature's News section to: newstips@nature.com

No bull: genes for better milk

On 13 January, the US Department of Agriculture (USDA) launched a service that allows dairy-cattle breeders to double their chances of selecting the

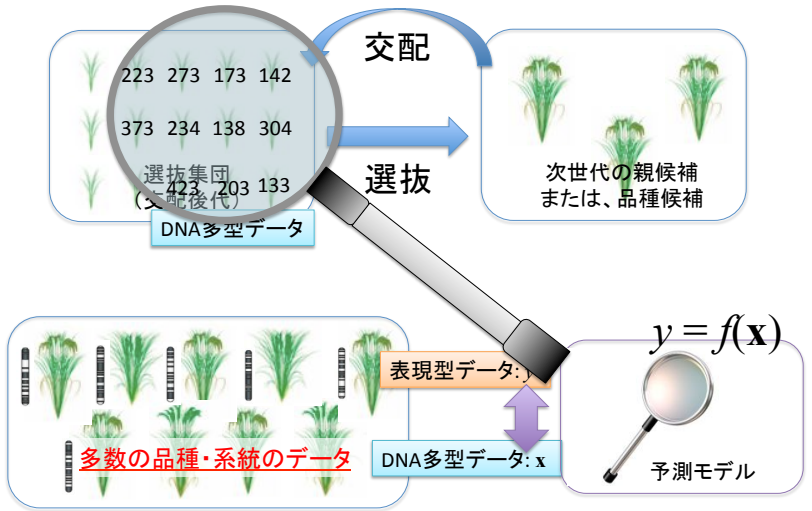
Using high-throughput analysis, the researchers could then compare the DNA from a young dairy bull against the chip SNPs, telling breeders which bull would be likely to sire calves that were good milk producers. The test costs about $225, and can be done when a bull is born, thus avoiding the $25,000–50,000 cost of raising a bull for five years to see if it sires good milk-producing offspring. "The best bulls become elite breeders," says Van Tassell, "The others become hamburger."

Curtis Van Tassell, a geneticist at the USDA's Bovine Functional Genomics Laboratory in Beltsville, Maryland. Working with Illumina Inc. of San Diego, California, Van Tassell's team created a microarray chip containing 54,000 genetic markers called single nucleotide

Rex Dalton

Published online 21 January 2009 | *Nature* **457**, 369 (2009) | doi:10.1038/457369a

Genomic selection (GS)



Phenotypingがボトルネックに

- The new bottleneck in this field has become **high throughput physiology and phenotyping** or **in '-omics' terminology, 'plant phenomics'**.
- This bottleneck is also apparent at the output end of plant biology, crop breeding.
- Marker assisted selection of high-yielding crop genotypes adapted to stressful environments is hampered by **slow, often subjective manual phenotyping, requiring laborious destructive harvesting across many field environments and seasons**.

Furbank 2009 Func Plant Biol 36:5

IMAGING

With 'Phenomics,' Plant Scientists Hope to Shift Breeding Into Overdrive

MELBOURNE, AUSTRALIA—Last May, a scrawny grass, *Brachypodium distachyon*, joined the e genomes ha podium may hood it is a p life cycle and chromosome pairs) that re modification superb mode and rice and t *Brachypodiu* tionize plant Enter pla ing techniq

world, consists of two nodes. One is a High Resolution Plant Phenomics Centre (HRPPC)

Mesophyll cells

work delivered enormous agricultural gains through the mid 1990s. But with yields of many crops having hit plateaus, green thumbs are no longer enough. Modern plant breeders need the equivalent of a watch-maker's magnifying glass and tweezers to tinker with complex and intertwined traits. Phenomics, says Uli Schurr, director of IPR, promises to usher in "precision agriculture

that helps plants resist osmotic shock.

Such mind-numbing screening will be automated and sped up when the Plant Accelerator roars to life. It will have a throughput of 2400 plants a day—10 times the capacity of current labs. Plants will travel by conveyer

Plant breeders are known for their "feel": the ability to select subtle traits that enhance a plant's performance.

…. But with yields of many crops having hit plateaus, green thumbs are no longer enough. Modern plant breeders need the equivalent of a watch-maker's magnifying glass and tweezers to tinker with complex and intertwined traits.

Finkel (2009) Science 325: 380

世界の潮流

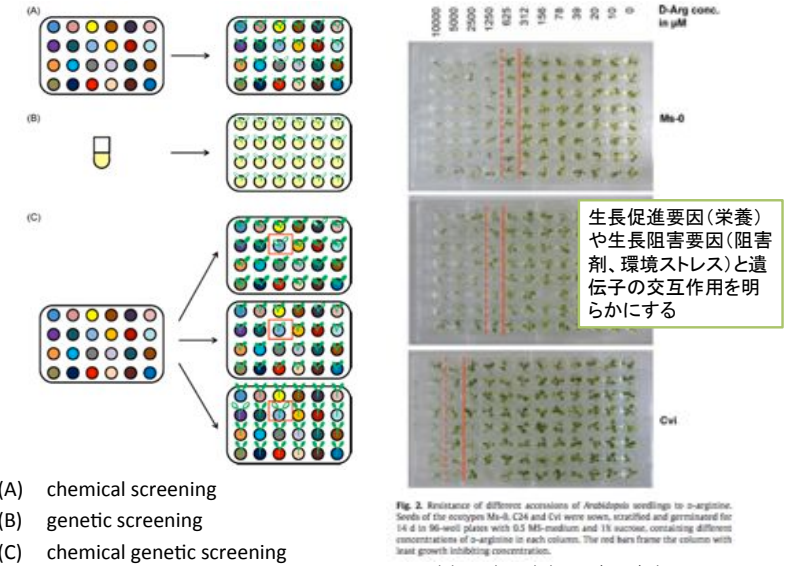
Phenomics facilities

in Gatersleben

International Plant Phenomics Network

Phenomicsで可能になる計測とは？

多検体を計測



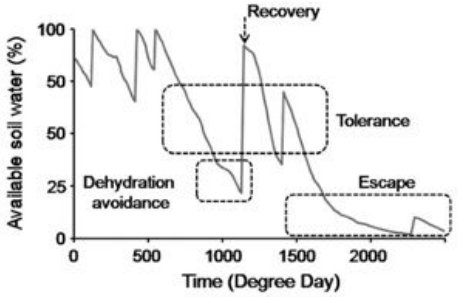
生長促進要因（栄養）や生長阻害要因（阻害剤、環境ストレス）と遺伝子の交互作用を明らかにする

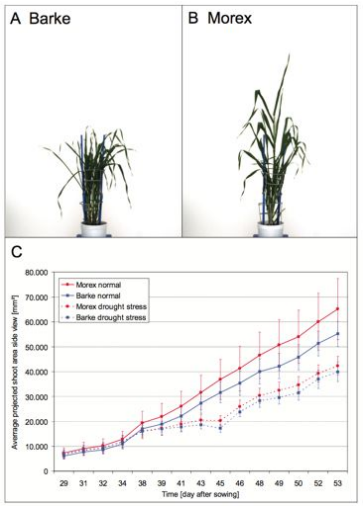
(A) chemical screening
(B) genetic screening
(C) chemical genetic screening

Fig. 2. Resistance of different accessions of Arabidopsis seedlings to D-arginine. Seeds of the ecotypes Ms-0, C24 and Cvi were sown, stratified and germinated for 14 d in 96-well plates with 0.5 MS-medium and 1% sucrose, containing different concentrations of D-arginine in each column. The red bars frame the column with least growth inhibiting concentration.

Kolukisaoglu and Thurow (2010) Plant Science 178:476

時系列で計測





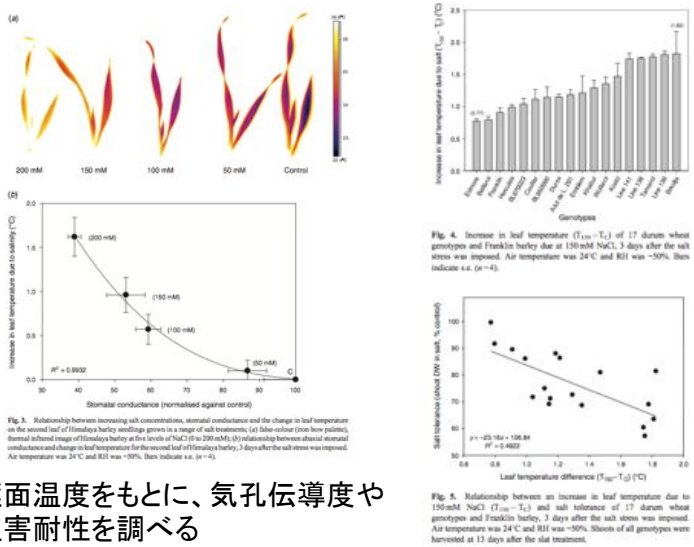
"Information about the physiological changes in response to drought over time is vital in order to identify and characterize the different drought-tolerance mechanisms."

→ 非破壊で同じ植物体を継続的に計測する必要性

Berger et al. (2010) J Exp Bot 61:3519

Hartmann et al. (2011) Bioinformatics 12:148

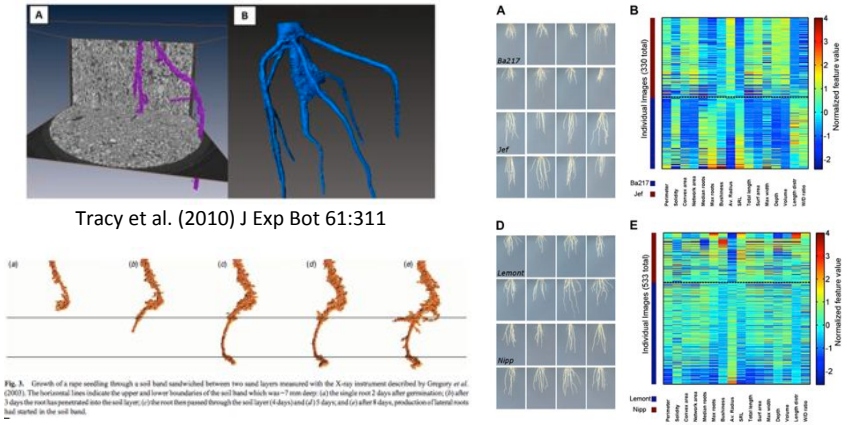
評価の難しい形質を計測



Sirault et al. (2009) Func Plant Biol 36:970

- 葉面温度をもとに、気孔伝導度や塩害耐性を調べる

見えにくいものを計測



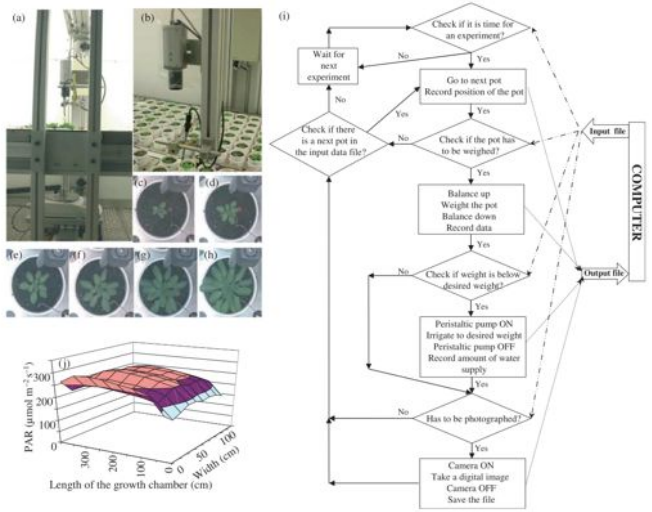
Tracy et al. (2010) J Exp Bot 61:311

Iyer-Pascuzzi et al. (2010) Plant Physiology 152:1148

- 根の形状を解析（NMR, X-ray CT, 透明培地など）

様々なスケールでのPhenomics

Phenomics in the laboratory



PHENOPSIS:　Granier et al. (2006) New Pytologist 169:623

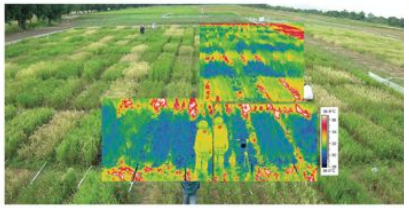
Phenomics in the green house

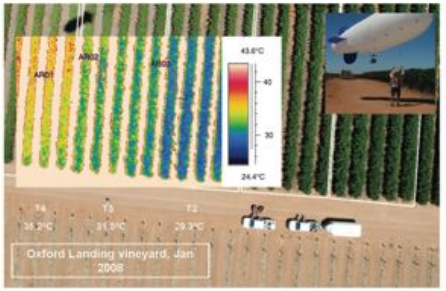
http://www.lemnatec.com/sites/default/files/application-sheets/2011/09/23/LemnaTec_Presentation_Varna_CMBPS.pdf

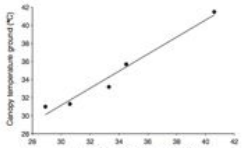
Figure 1 View of the automatic greenhouse system. Image acquisition device for images in visible, near-infrared and ultra-violet spectra (left), greenhouse device consisting of a conveyor belt system carrying 312 barley plants (right).

Hartmann et al. (2011) Bioinformatics 12:148

Phenomics in the field



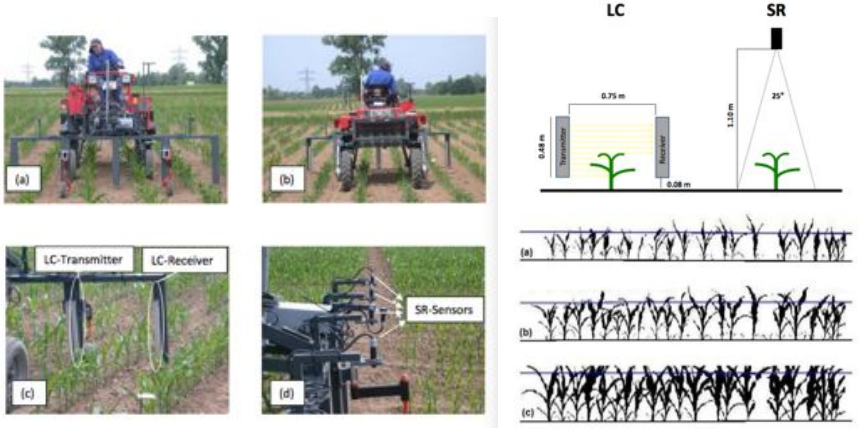




タワーや小型飛行船を利用したリモートセンシング

Jones et al. (2009) Func Plant Biol 36:978

Phenomics in the field



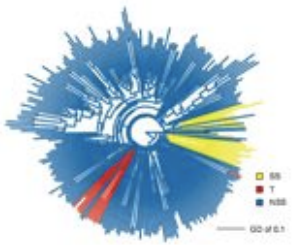
Laser curtain

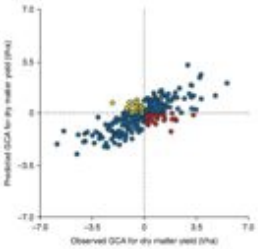
Montes et al. (2011) Field Crops Research 121:268–273

Riedelsheimer et al. (2012) Nature Genetics 44:217

Genomic and metabolic prediction of complex heterotic traits in hybrid maize

Christian Riedelsheimer[1], Angelika Czedik-Eysenberg[2], Christoph Grieder[1], Jan Lisec[2], Frank Technow[1], Ronan Sulpice[2], Thomas Altmann[3], Mark Stitt[2], Lothar Willmitzer[2,4] & Albrecht E Melchinger[1]





285デント系統を2つのフリントテスターに交配して一般組合せ能力（GCA）を計測
56,110 SNPsおよび130 metabolitesを用いてGCAを予測（精度：0.72-0.81, 0.6-0.8）

Phenomics in the forest

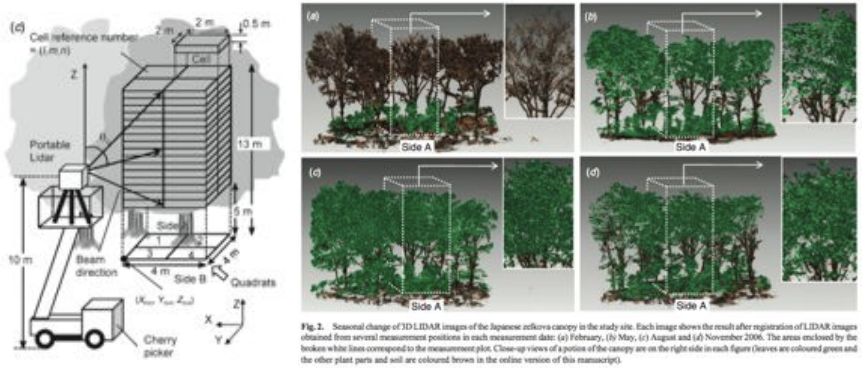


Fig. 2. Seasonal change of 3D LIDAR images of the Japanese zelkova canopy in the study site. Each image shows the result after registration of LIDAR images obtained from several measurement positions in each measurement date: (a) February, (b) May, (c) August and (d) November 2006. The areas enclosed by the broken white lines correspond to the measurement plot. Close-up views of a portion of the canopy are on the right side in each figure (leaves are coloured green and the other plant parts and soil are coloured brown in the online version of this manuscript).

Light Detection And Ranging (LIDAR) imaging
ケヤキのLAIの季節変動を計測
平均平方誤差0.26 m^2 m^{-3}

Hosoi and Omasa (2009) *Functional Plant Biology* **36:** 998–1005

Phenomicsデータの蓄積は？

Phenome DBの例: PHENOPSIS DB

- PHEONPSISを用いて自動収集されたArabidopsis thalianaの画像や表現型データが、実験プロトコルや実験メタデータ（環境条件など）とともに提供されている
- 画像解析や統計解析のためのスクリプトも提供されている

環境データも必要！
Environmental Omics

データ収集だけでなく
統合的モデル化も肝！

ゲノム、環境、表現型

＜解決すべき重要課題＞
地球規模の環境変動と
資源崩壊下での
食料生産の増大

三つ巴の関係の
理解が不可欠

圃場

Environmental omics

圃場を学際的共同研究の場に!

Phenomics

Genomics

Information collection
情報の網羅的収集
フェノミクス、ゲノミクス、
環境オミックス

Integrative modeling
統合的モデル化
フィールドインフォマティクス、
バイオインフォマティクス

Implementation
食糧問題
エネルギー問題の解決へ
環境適応品種
革新的栽培技術