The NBER Productivity Program
Presentation to Board of Directors
Ernst R. Berndt, MIT Sloan and NBER
September 13, 2010

Agenda

- Brief History

- Working Paper Publication History

- Current Membership and Affiliation, Source of Ph.D. Degree

- Discussion of Selected Recent Research Themes – Illustrated by Four Recent Working Papers, and Role of Productivity Program

Brief History: I

- Productivity program first of a long line of NBER focused field programs for which university Ph.D. programs did not have field qualifying examinations – initiated in 1977
- Zvi Griliches Director from 1977 to 1999, Ernst Berndt named Acting Director in 1999, Director in 2000
- Nicholas Bloom, Stanford, and Joshua Lerner, HBS, become Co-Directors January 1, 2011

Brief History: II

- Reflecting Griliches' deep interest in the measurement and quantification of factors affecting productivity growth, a principal research focus has long been on productivity measurement, R&D, returns to education, diffusion of new technologies, patenting, entrepreneurship and innovation

- The Productivity Program measurement focus has involved close cooperation with and support of the Conference on Research in Income and Wealth (CRIW), whose membership includes numerous government economists and statisticians, as well as economists in the private sector

- NBER/CRIW collaborations include joint Summer Institute meetings, workshops, and conferences that have resulted in numerous "Orange Cover" *Studies in Income and Wealth* volumes, now published by the University of Chicago Press

Productivity Program Research Publications

- Between 1977 and September 1, 2010, there have been 1,111 NBER Working Papers in Productivity – some by non-productivity program authors – out of NBER total of about 16,300
- The annual number of productivity working papers averaged 8.8 between 1977 and 1990, 23.4 from 1991-95, 46.2 between 1996-2000, 59.5 from 2001-5, and 70.75 between 2006-9
- Through 9/1/10, 60 productivity working papers, annualized to 90 for entire year (but no seasonal adjustment)

Number of Productivity Program Working Papers, 1977 - 2010
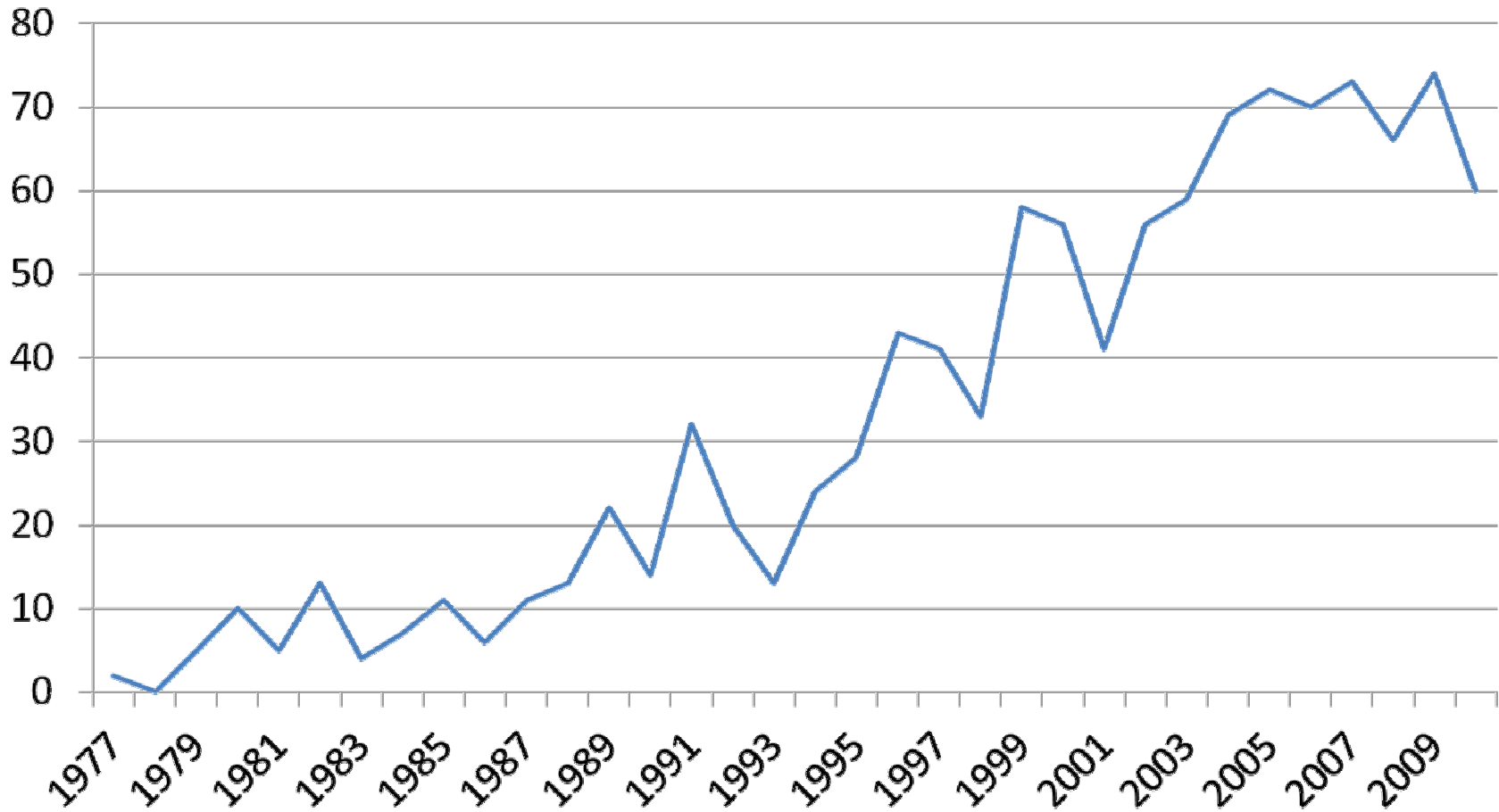
Productivity Program Researchers

- Currently there are 59 researchers who have their primary affiliation with the productivity program -- 14 Faculty Research Fellows and 45 Research Associates
- These numbers have been relatively stable over the last decade, perhaps increasing slightly between 2000-2005
- The 45 RAs received their Ph.D. at 16 different universities, and currently have their primary academic appointment at 29 different universities
- For FRFs, these numbers are seven and 11, respectively
- Overall, the 59 productivity program affiliates have Ph.D.s from 19 distinct universities, and have their primary academic appointments at 33 different universities
- In addition, 23 academics have a secondary FRF/RA appointment in the productivity program – and 22 productivity program members have a secondary appointment in at least one other NBER program

Recent Productivity Working Papers

- John Haltiwanger, Ron S. Jarmin and Javier Miranda, "Who Creates Jobs? Small vs. Large vs. Young", WP #16300, August 2010

- Heidi Williams, "Intellectual Property Rights and Innovation: Evidence from the Human Genome", WP #16213, August 2010

- Mark Trusheim, Murray L. Aitken and Ernst R. Berndt, "Characterizing Markets for Biopharmaceutical Innovations: Do Biologics Differ from Small Molecules?", WP # 16014, May 2010

- Xi Chen and William D. Nordhaus, "The Value of Luminosity Data as a Proxy for Economic Statistics", WP # 16317, August.

Who Creates Jobs?
Small vs. Large vs. Young

by

John Haltiwanger, University of Maryland and NBER

Ron S. Jarmin, U.S. Census Bureau

Javier Miranda, U.S. Census Bureau

Literature and Skepticism

- Literature exists linking *growth rate* of establishment (firm?) employment to size *level* of establishment/firm (e.g., 1-4, 5-9,…,5000-9999, 10000+ employees) – finds inverse relationship
- Statistical and classification issues:
  - Regression to the mean
  - Net vs. gross, job creation and destruction
  - Start-up vs. old small firms, "up and out" of start-ups
  - Establishment vs. firm, accounting for births, continuing, mergers and acquisitions, and deaths/exits

Definitions and Issues

- An *establishment* is a specific physical location where business activity occurs while a *firm* reflects all the establishments under common operational control – need to link them, look at organic growth of establishments based on size and age of the parent firm

- For growth rate calculation between t-1 and t, use t-1 (base), t(current) or average in denominator? For classifying into size class, have problem of regression to the mean – base generates negative spurious, current positive spurious calculation.   Why? Authors recommend use of the "current-average" of t and t-1 to assign firm to size class, but acknowledge sensitivity.

Regression to the Mean

- "Businesses that recently experienced negative transitory shocks (or even a transitory measurement error) are more likely to grow while businesses recently experiencing positive transitory shocks are more likely to shrink. This effect alone will yield an inverse relationship between size [in base year] and growth." Similarly, use of current year generates positive bias. Authors use the mean employment in the two time periods to assign firm class size.
- Gibrat's Law: Growth rate is independent of size

Contributions of This Paper

- Uses rich longitudinal information from the Census Bureau's *Business Dynamics Statistics* and its source file, the *Longitudinal Business Database*
- Emphasizes the role of firm age and firm births in accounting for net and gross job flow patterns – young (not necessarily small) firms display both disproportionate job creation and job destruction, and are generally smaller than older firms
- Older firms grow (decline) by adding (exiting) establishments, younger firms by adding (destroying) jobs within establishments
- Documents importance of regression to the mean

Creative Destruction in U.S.

Average Annual Rates from 1977 to 2005
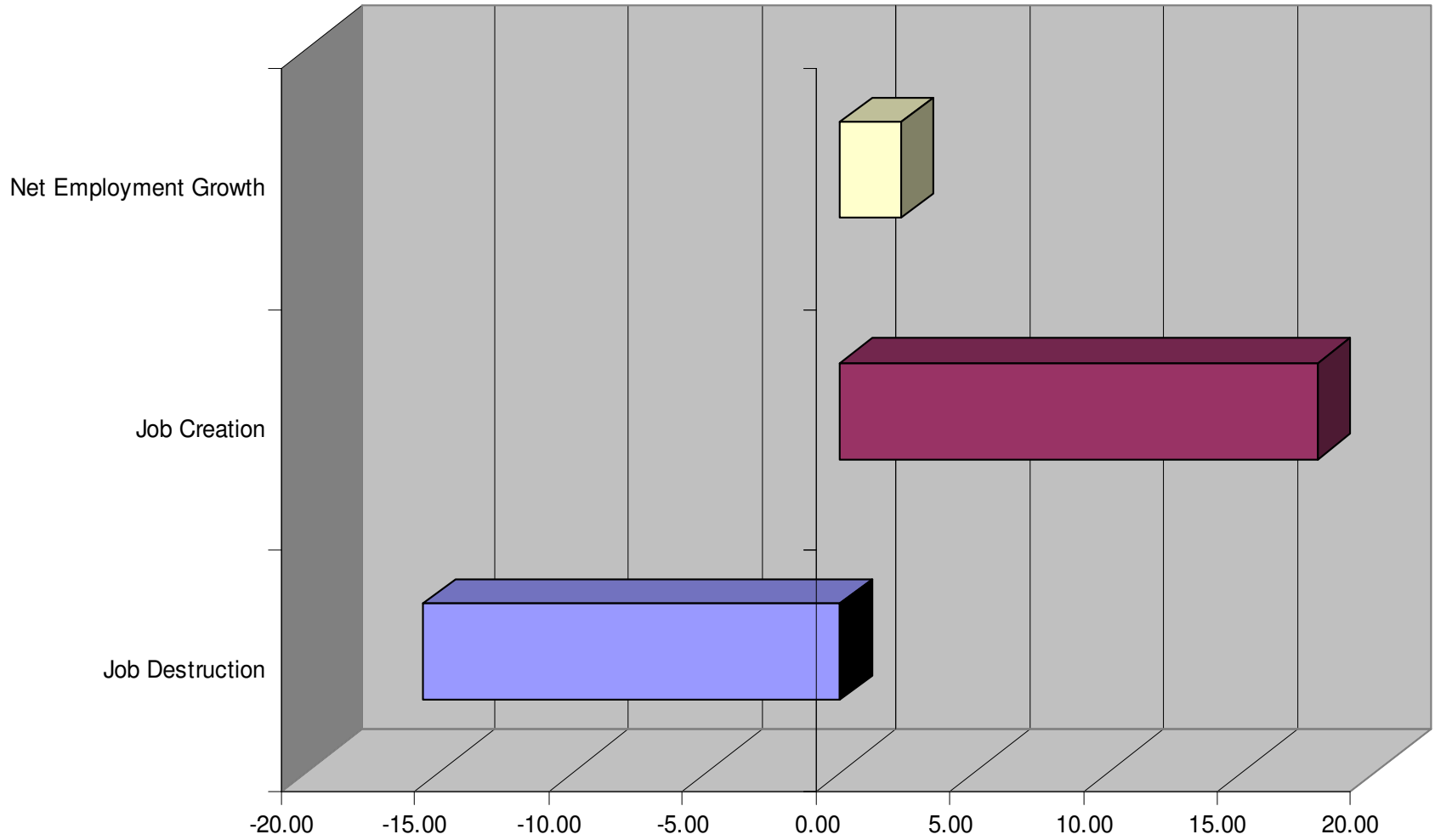
Business Startups as Percentage of Employment and Net Growth

Percent

160	
140	
120	
100	
80	
60	
40	
20	
0	

Share of Employment Share of Net Growth
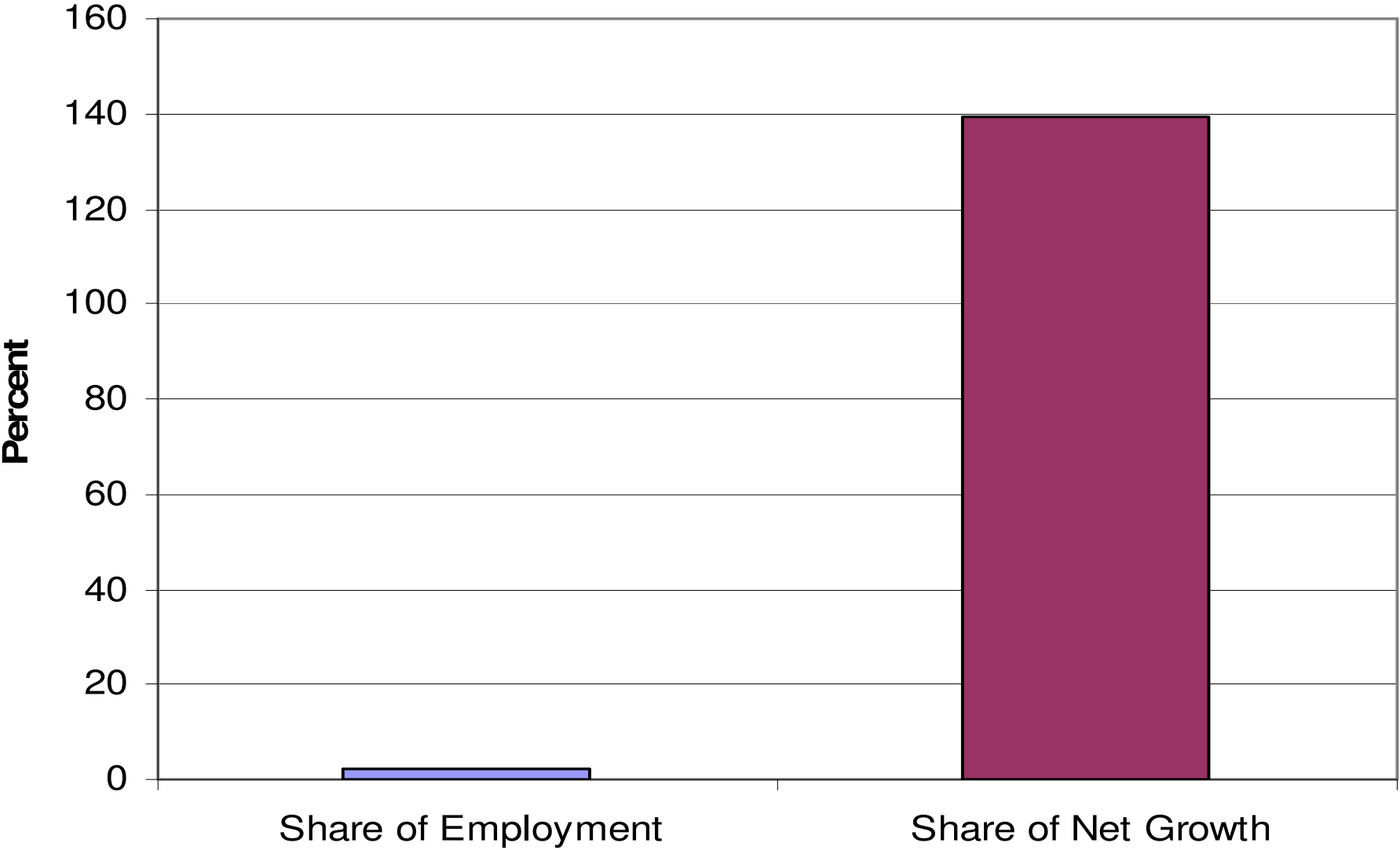
Shares of Employment, Job Creation and Destruction by Firm Size and Age Broad Classes
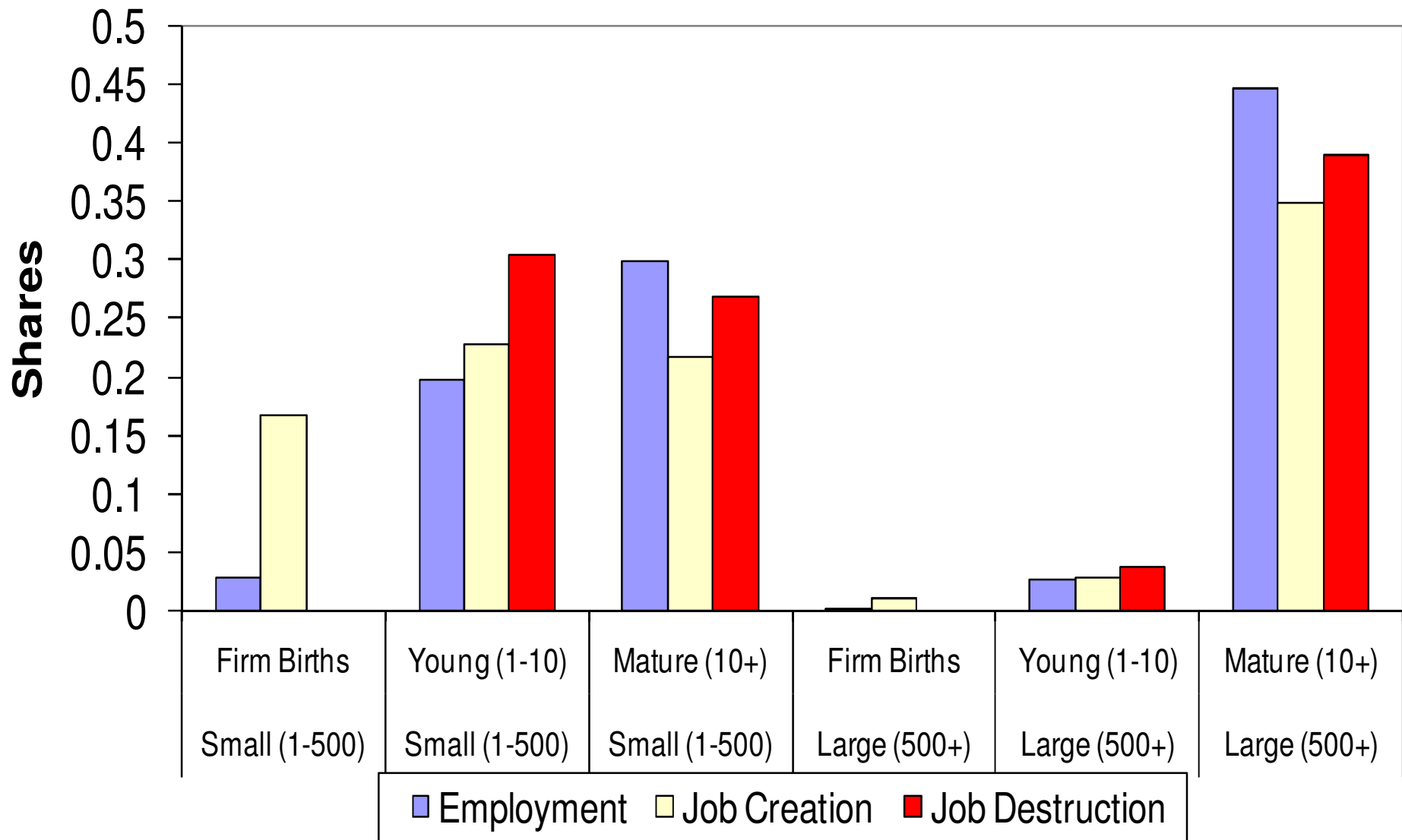
The Size/Age Relation

Share of Startups within Firm Size Class
Current Firm Size, Average 1992-2005
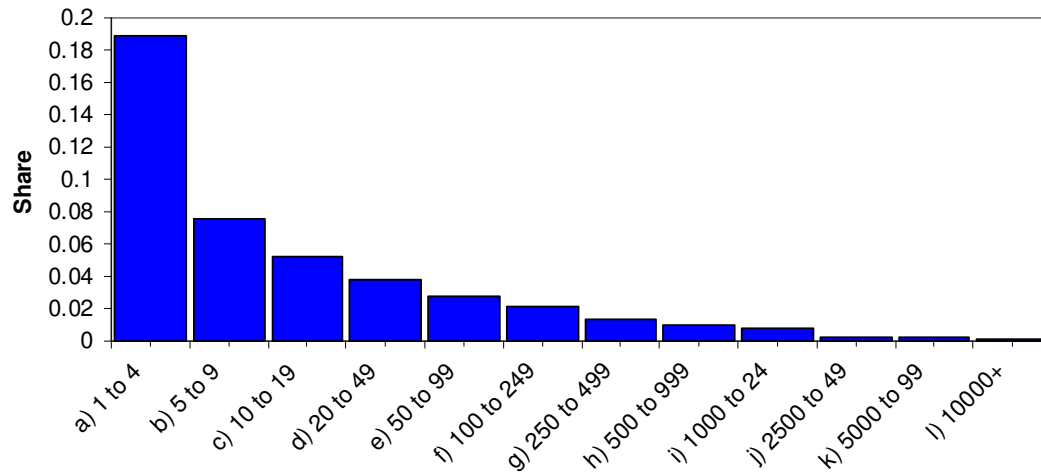
Firm startups are small.
Larger firms are older

Average Firm Age by Firm Size,
Continuer firms in 2005, Employment Weighted

"Up or Out" dynamics play critical roles….

Productivity Relative to Mature Surviving Incumbents
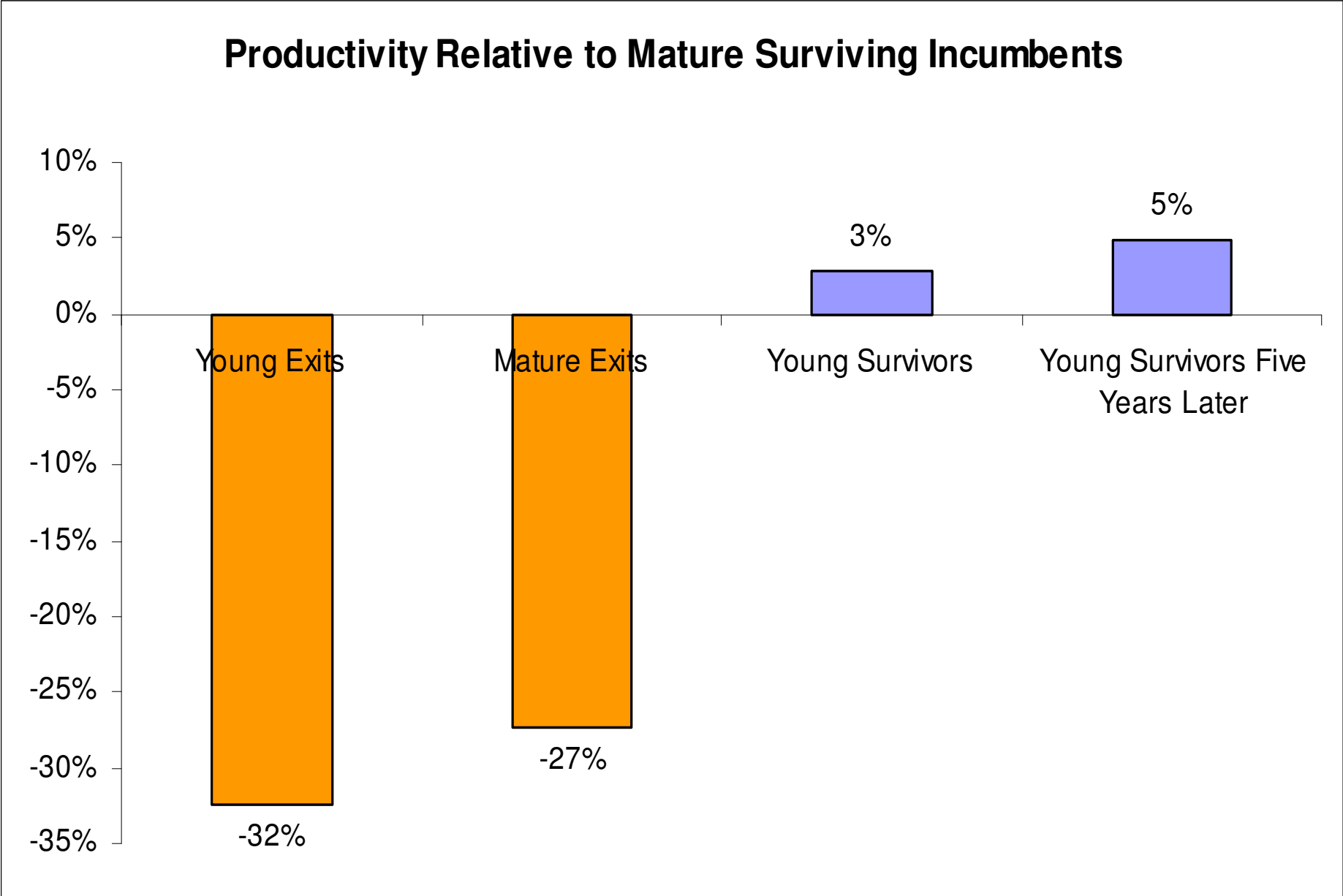
Authors' Interpretation
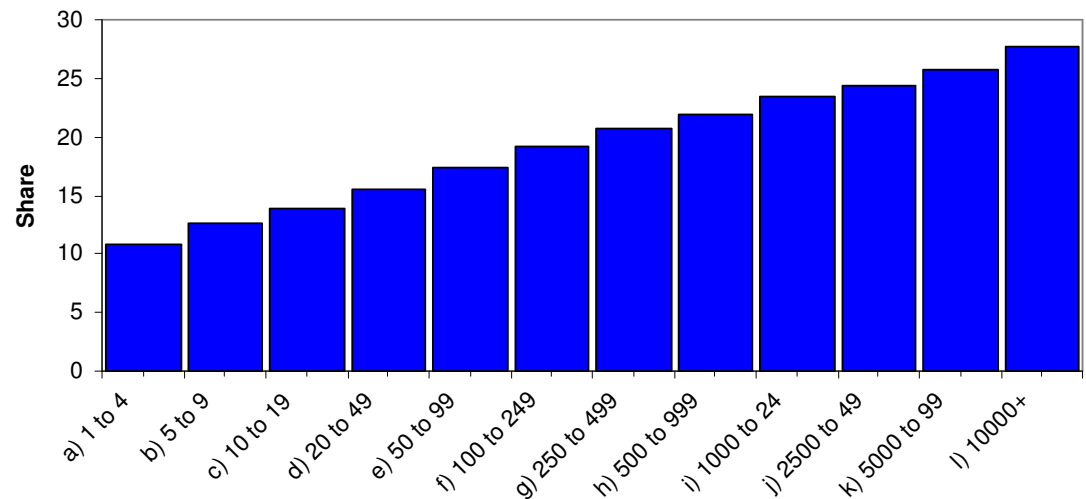
- More nuanced view of role of small businesses as "primary creators of jobs"?
  - More informative to focus on firm startups and firm age
    - Firm startups contribute substantially to gross and net job creation
    - Firm startups tend to be small
    - Young firms very volatile (up or out)
    - Firm age patterns don't yield patterns that can be misinterpreted given regression to the mean effects
- Firm startup and firm age contributions to job growth consistent with models of industry evolution that stress importance of firm entry, learning, experimentation and selection
  - Dominant role of idiosyncratic factors
- Interpret current economic trends through this lens:
  - Did recent financial collapse adversely impact these young/small firm dynamics?

Intellectual Property Rights and Innovation: Evidence from the Human Genome

Heidi Williams

NBER and MIT*

Working Paper No. 16213

August 2010

Introduction

- Intellectual property (IP): one policy tool to promote R&D
- Focus in this paper: impact of IP on subsequent R&D
  - *Ex post* monopoly control could discourage subsequent R&D
  - More recent arguments: IP could *encourage* subsequent R&D
  - Net effect ambiguous from a theoretical perspective
- Facilitated by cumulative gene ID biologist recorded progress – can track history
- Empirical challenge: selection of technologies into having IP
- Contributions of this research:
  - Isolate variation in IP across otherwise similar technologies
  - Estimate impact of IP on subsequent R&D

Empirical context: Sequencing of the human genome

- Public Human Genome Project and private firm Celera
  - DNA sequencing methods induced:
    - Variation in which effort first sequenced a gene
    - Variation in IP across the human genome

- Construct three research designs from this empirical context
  - Do Celera genes differ in innovation outcomes as of 2009?
    - Relative to *ex ante* similar genes always in the public domain
  - Did *removal* of Celera's IP affect within-gene innovation flows?
  - Focus on variation in length of time a gene was held with Celera's IP

- Newly-constructed gene-level data set
  - Traces the transition of genes "from lab to market"
  - Measures both scientific research and product development

Conceptual framework

- Why might IP hinder subsequent innovation?
  - Potential imperfections in cross-firm contracting
    - Coase (1960), Green and Scotchmer (1995), Bessen (2004)
    - Murray and Stern (2007), Murray *et al*. (2008)
    - Walsh, Arora, and Cohen (2003)
  - Diversity of experimentation: Aghion *et al.* (2008)

- Why might IP encourage subsequent innovation?
  - *Ex post* justifications for IP: *e.g.* Kitch (1977)
  - Imperfect IP protection in downstream markets
    - Policy argument made in favor of US Bayh-Dole Act
    - Relevant for medical diagnostic markets

The sequencing of the human genome

- 1990: Human Genome Project (HGP)
  - Led by James Watson, later Francis Collins; deadline of 2005
- May 1998: Celera
  - Led by Craig Venter; deadline of 2001
- 2001: publication of draft genomes in *Nature* and *Science*
- 2003: public sequencing effort declared "complete"

Intellectual property strategies

- Human Genome Project: Bermuda Rules
  - Required nightly submissions to public online database
  - Motivations:
    - HGP (1996): encourage R&D; maximize social welfare
    - Eisenberg (2000): discourage patenting (by HGP and others)
- Celera's IP
  - Applied to genes sequenced first by Celera
  - Package of IP/contract law tools (details in paper)
  - Removed when Celera genes were re-sequenced by HGP

Conceptual issues in data construction

- Track economically relevant outcome variables at genotype-phenotype level (relevant to human health)
- Construct data at the level of naturally occurring biological molecules that can be precisely identified at various stages of R&D
- Use the same data sets used by scientific researchers, MDs
- All data collected in a 2009 cross-section
  - For two outcomes, can construct retrospective cross-sections

Summary statistics for gene-level data

	mean	std dev	min	max
Panel A: Celera intellectual property (IP)				
celera: 0/1, had Celera IP	0.060	0.238	0	1
Panel B: Outcome variables				
publications: publications in 2001–2009	2.197	9.133	0	231
uncertain_phenotype: uncertain phenotype	0.453	0.498	0	1
certain_phenotype: certain phenotype	0.081	0.273	0	1
test: 0/1, used in any diagnostic test	0.060	0.238	0	1
$N = 27{,}882$				

Notes: See Table 1 in paper. Gene-level observations. Full sample of genes ($N = 27{,}882$).

Cross-section results: Summary

- Celera genes have ~30 percent lower scientific research and product development outcomes as of 2009
    - 35 percent fewer publications from 2001-2009 (mean = 1)
    - 16pp less likely to have a known, uncertain phenotype link (mean = 30%)
    - 2pp less likely to have a known, certain phenotype link (mean = 4%)
    - 1.5pp less likely to be used in a currently available diagnostic test (mean = 3%)

Panel: gene-year publications
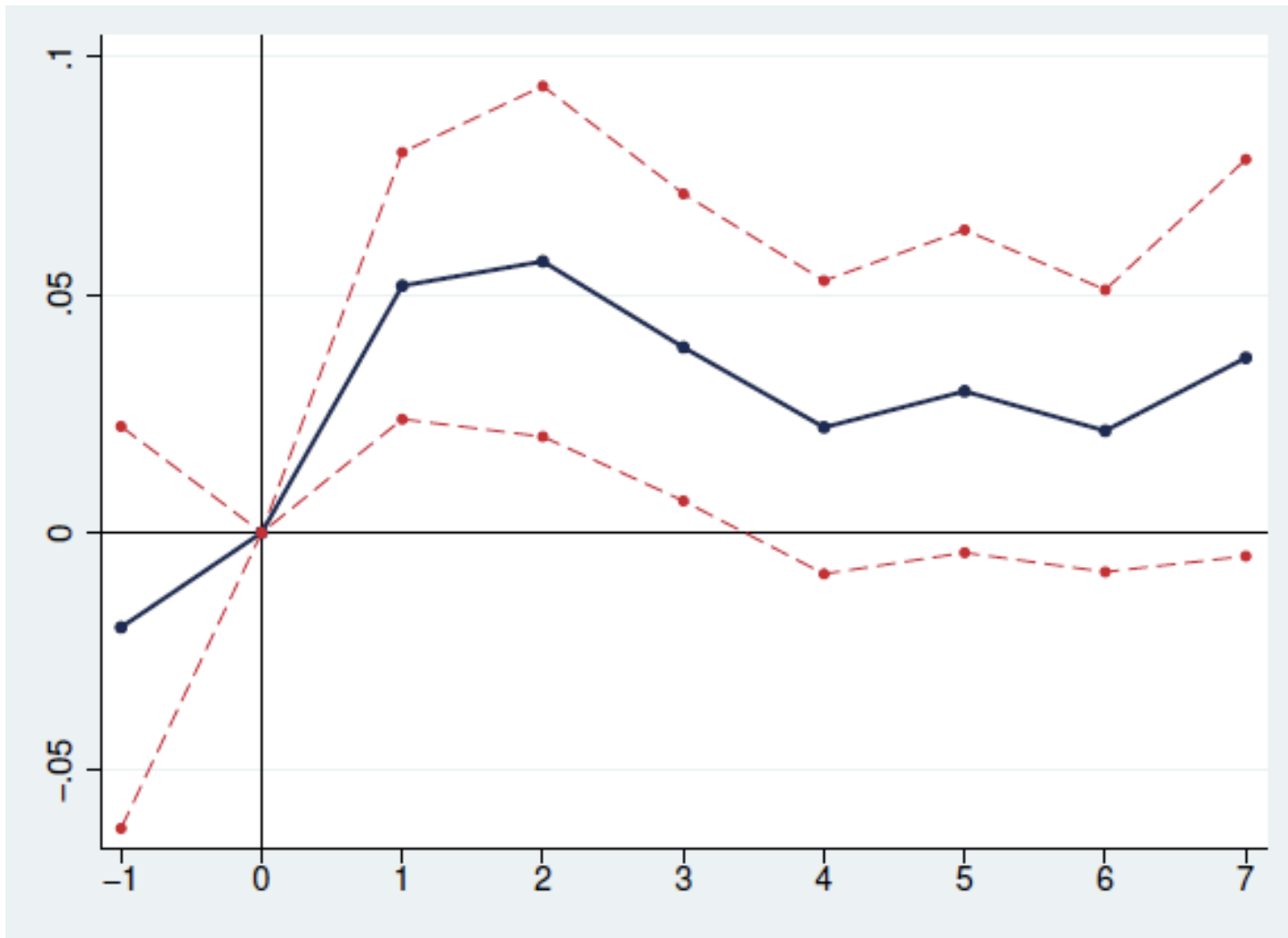
Panel results: Summary

- Within-gene flows of innovation increased ~30 percent after Celera's short-term IP was removed
  - Event study graphs suggest persistent increases

Conclusions

- Intellectual property is a widely-used policy to promote R&D
- Relatively little known about how IP impacts subsequent R&D
- Evidence from the sequencing of the human genome
  - Variation in IP across otherwise similar technologies
  - Genes with IP have ~30 percent less subsequent R&D
- Results are one input into broader questions about IP systems
  - Counterfactual: placing Celera genes in the public domain
  - *E.g.* Patent buyout-type mechanism (Kremer 1998)

Characterizing Markets for Biopharmaceutical Innovations: Do Biologics Differ From Small Molecules?

by

Mark R. Trusheim

Murray L. Aitken

Ernst R. Berndt

Motivation

- Recent publicity regarding the confluence of biologics and small molecules:
  – Biosimilars legislative debate accompanied by the release of multiple influential studies
  – High profile mergers of classic small molecule pharmaceutical firms with Biologic emphasizing firms
  – The return of vaccine products and company strategies
- Relatively little data driven analysis of biologic and small molecule commercial (rather than development and regulatory) experiences

Commercial Stage Presents Dual Research Opportunity

- Measure Prior Pipeline Performance
  - Number and composition of new product launches
  - Relative innovation as measured by NDAs/BLAs, orphan designations and supplemental approvals
  - Relative safety performance as measured by FDA black box warnings
- Determination of Relative Marketplace Similarity or Difference
  - Diffusion of new technology (adoption) as measured by sales and sales growth
  - Market position and life cycles as measured by sales and pricing patterns from launch

Approach Focused on Recent Product Experience

- 1998-2008 universe of novel NDA/BLA therapeutic products launched in the United States
  - Market experience over the period
  - FDA experience over life of product
- Objective descriptive analytical methods employed
  - Inflation adjustment by GDP deflator
  - All products time series aligned by time relative to launch date, NOT calendar date
  - All products equal approach: Individual product analyses, generally not weighted by sales.

Scientific, Development and Regulatory Production: Number and Composition of Product Launches 98-08

- 308 total biopharmaceuticals launched -- 212 small molecules and 96 biologics

Number of Newly Launched New Molecular Entities, Small Molecules and Biologics, 1998-2008

	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008
Small Molecule	32	29	25	18	20	16	15	14	17	16	10
Biologic	14	7	6	13	8	14	6	6	10	3	9
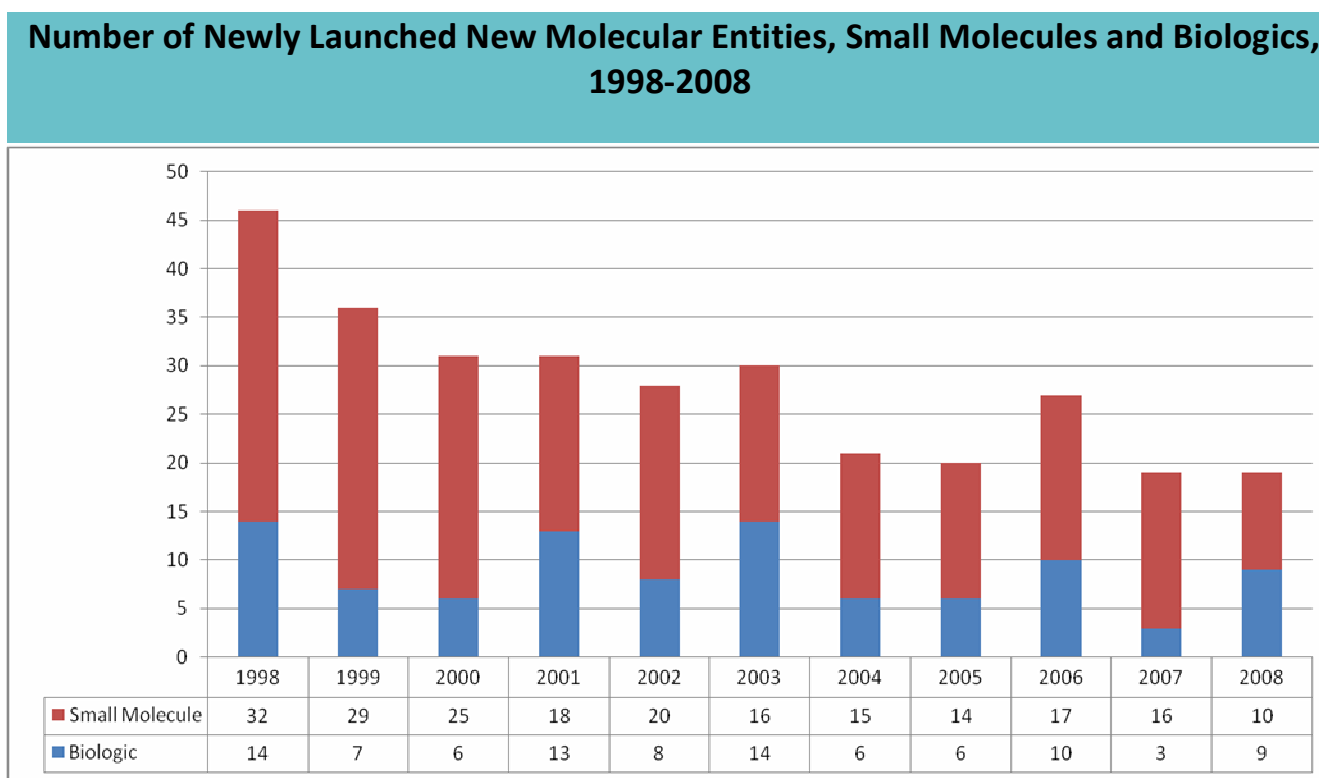
Biologics Concentrated in Four Areas, with Presence in Most Classes

- 61% of biologics in four areas
- No biologics in only three top level therapeutic classes

Therapeutic Class Composition of Biopharmaceutical Innovations: Biologics and Small Molecules			
ATC Classification	Biologic	Small Molecule	Total
A: Alimentary Tract and Metabolism	16	26	42
B: Blood and blood forming organs	16	6	22
C: Cardiovascular System	1	20	21
D: Dermatologicals	3	5	8
G: Genito-Urinary Systems and Sex Hormones		13	13
H: Systemic Hormonal Preparations, Excl. Sex Hormones And Insulins	7		7
J: Anti-Infectives For Systemic Use	23	38	61
K: Intravenous Solutions		1	1
L: Antineoplastic And Immunomodulating Agents	21	28	49
M: Musculo-Skeletal System	4	6	10
N: Nervous System	1	36	37
P: Antiparasitic Products		1	1
R: Respiratory System	1	11	12
S: Sensory Organs	2	10	12
V: Various	1	11	12
Total	96	212	308

Innovation Distinctions Using Surrogate Measures

- Biologics nearly twice as likely to be designated Orphan Drug status
- Both small molecules and biologics have high priority review rates
- Number of supplemental indications similar, slightly greater for biologics

Orphan, Priority and Supplemental Reviews			
	Biologic	**Small Molecule**	**Grand Total**
Orphan			
Number	23	28	51
Percentage	24%	13%	17%
Priority Review			
Number	42	82	124
Percentage	44%	39%	40%
Mean Supplementals	0.77	0.66	0.69
Total Therapeutics	96	212	308

Safety Experiences Similar as Measured by Warning and Exit Experiences

- Biologics have modestly higher black box warning rate, but also concentrated in oncology and high tolerance indications
- Exits include withdrawals for all reasons
- Vaccines account for three of seven biologic withdrawals

Safety: Black Box Warning Experience			
	Biologic	Small Molecule	Total
Number	25	42	67
Percent	26%	20%	22%

Product Exits			
	Biologic	Small Molecule	Total
Number	7	20	27
Percent	7.3%	9.4%	8.8%

Distinctive Pricing Dynamics of Biologics and Small Molecules

Mean Real Price Growth (Quarter over Prior Year's Same Quarter) from First Quarter of Observed Revenues
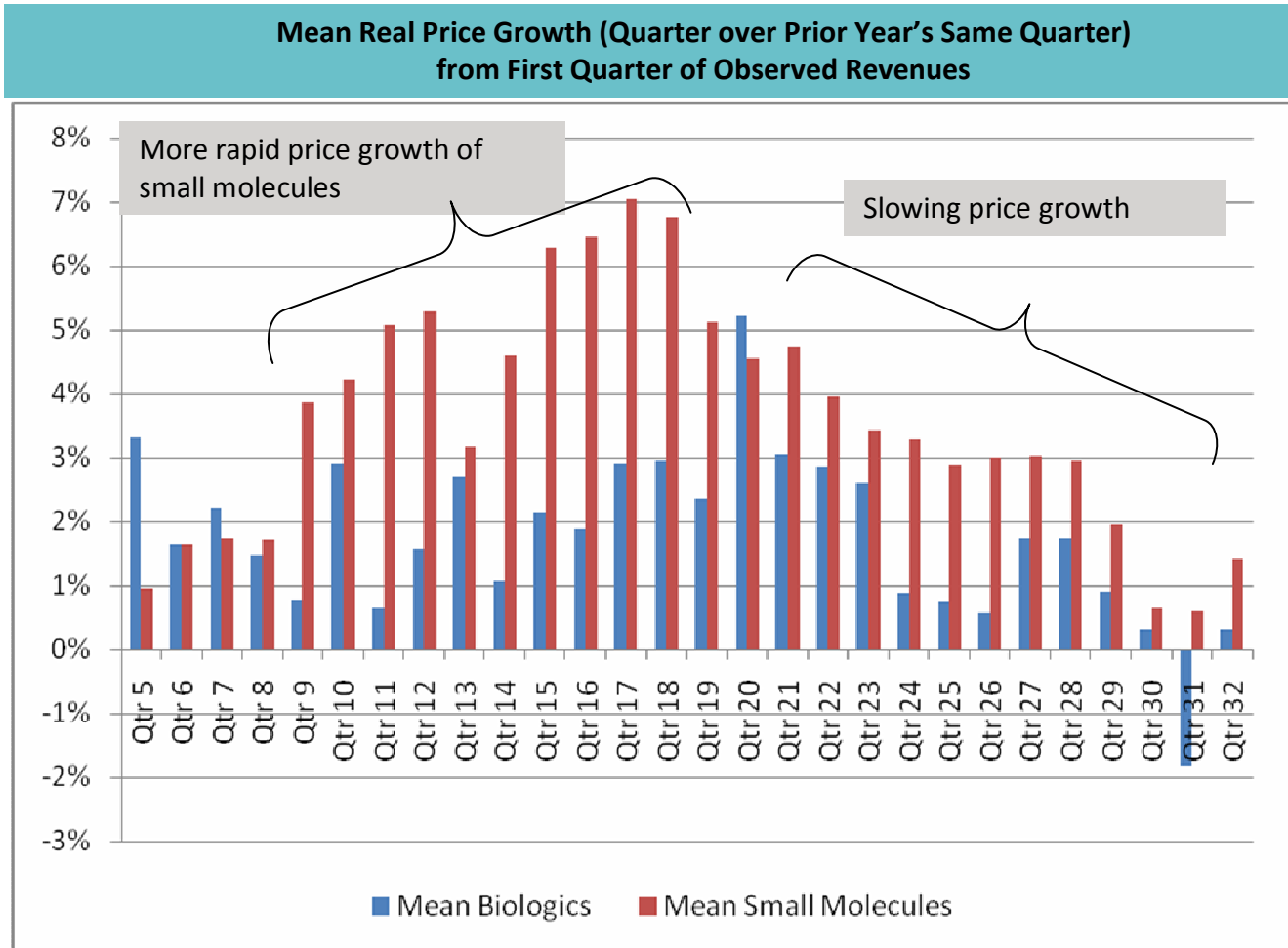
Differing Revenue Dynamics of Biologics and Small Molecules

Mean Inflation Adjusted Sales from First Quarter of Observed Revenues, All ATC Classes, Biologics and Small Molecules
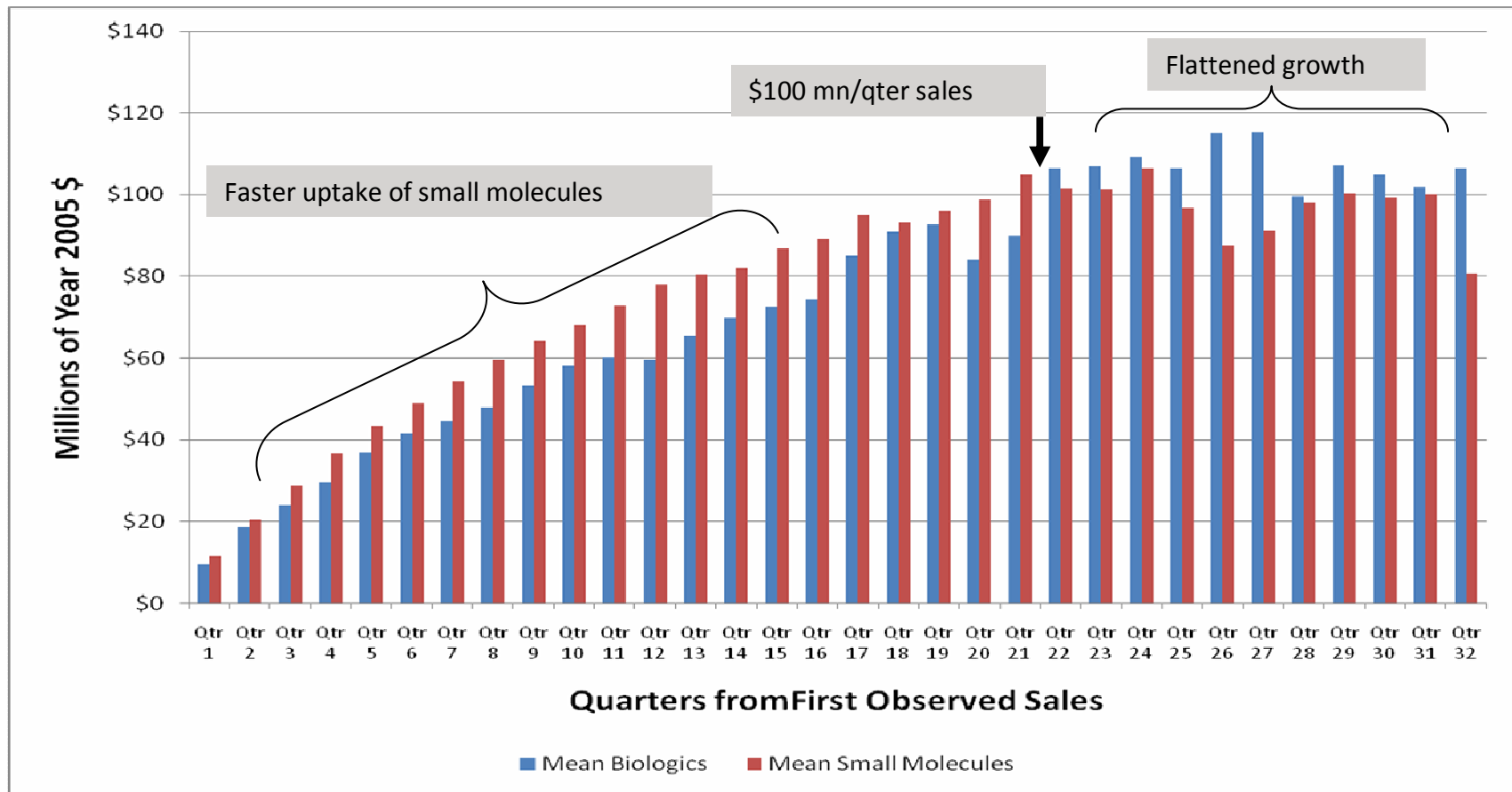
Conclusions

- Commercial experience of biologics appears quite distinct from that of small molecules – no generic cliff?
- The future commercial environment is fluid
  - Biologics may become 50% or more of future product launches
  - Combined biopharma firms with both small molecule and biologic portfolios are becoming more common and larger
- The market dynamics will likely vary by therapeutic area
  - Solution
  - Suspension
  - Separation

The Value of Luminosity Data as a Proxy for Economic Statistics

Xi Chen

William D. Nordhaus

Yale University

Joint CRIW-NBER Summer Institute Session

Cambridge, Massachusetts

July 19 – 20, 2010

Results written up in NBER Working Paper 16317, August 2010

Issues in GDP measurement and our motivation

We have been developing G-Econ data set with gridded GDP at 1 °C x 1 °C resolution for all terrestrial grid cells

Have observations for 27,000 grid cells for 4 years

Data are very poor for countries with:

- weak statistical systems

- sparse regional data

Question for this project: Can we use luminosity (nighttime lights) data as a proxy for standard accounting data for low-quality regions?
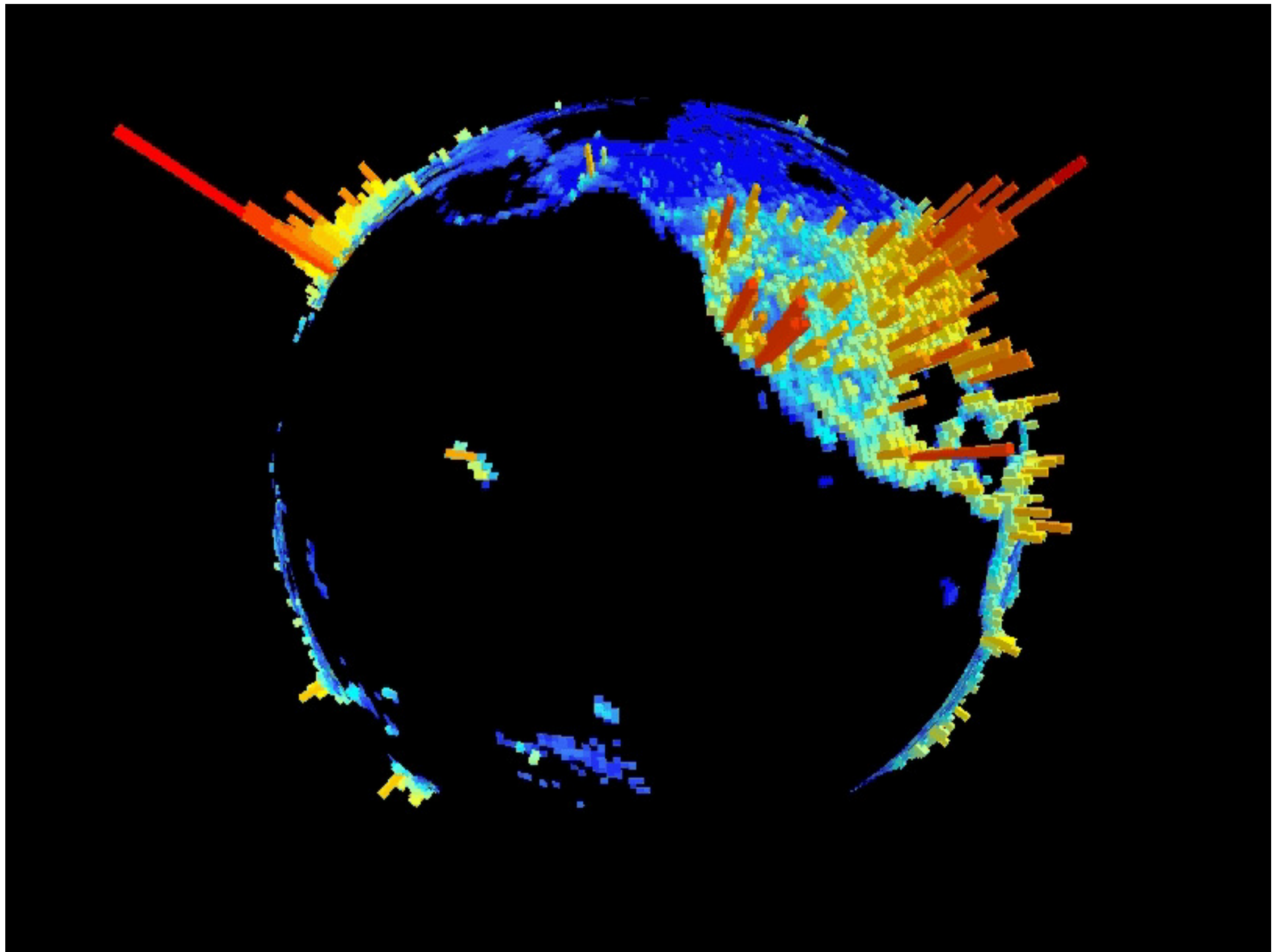
The Value of Luminosity Data as a Proxy for Economic Statistics

Xi Chen
William Nordhaus

Key elements in evaluating luminosity as a proxy

The key elements in determining the value of a proxy are:

1. The quality of the luminosity data
2. The errors of measurement of the standard GDP data
3. The statistical relationship between luminosity and GDP

Overglow areas

I-15 Interstate traffic
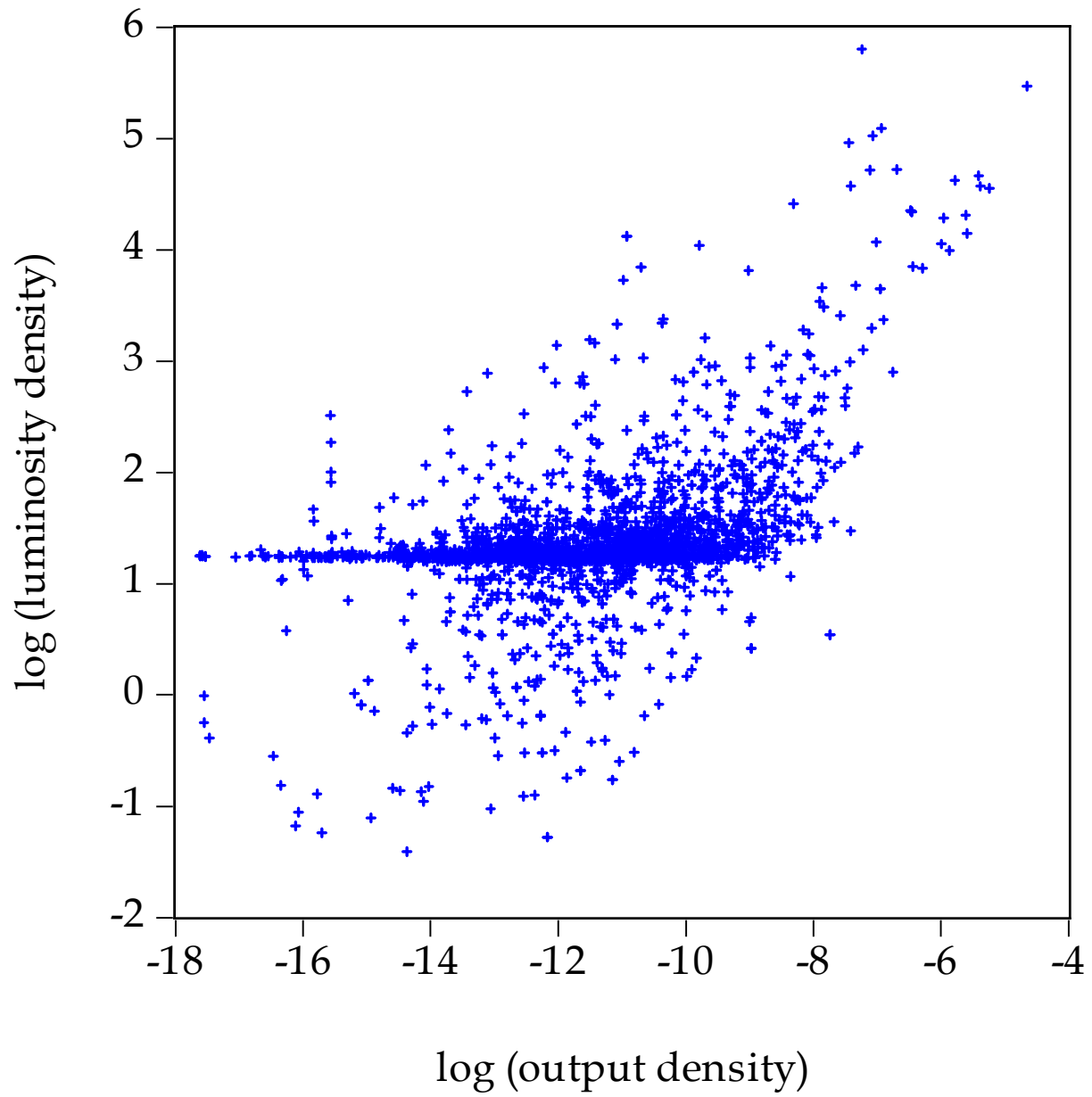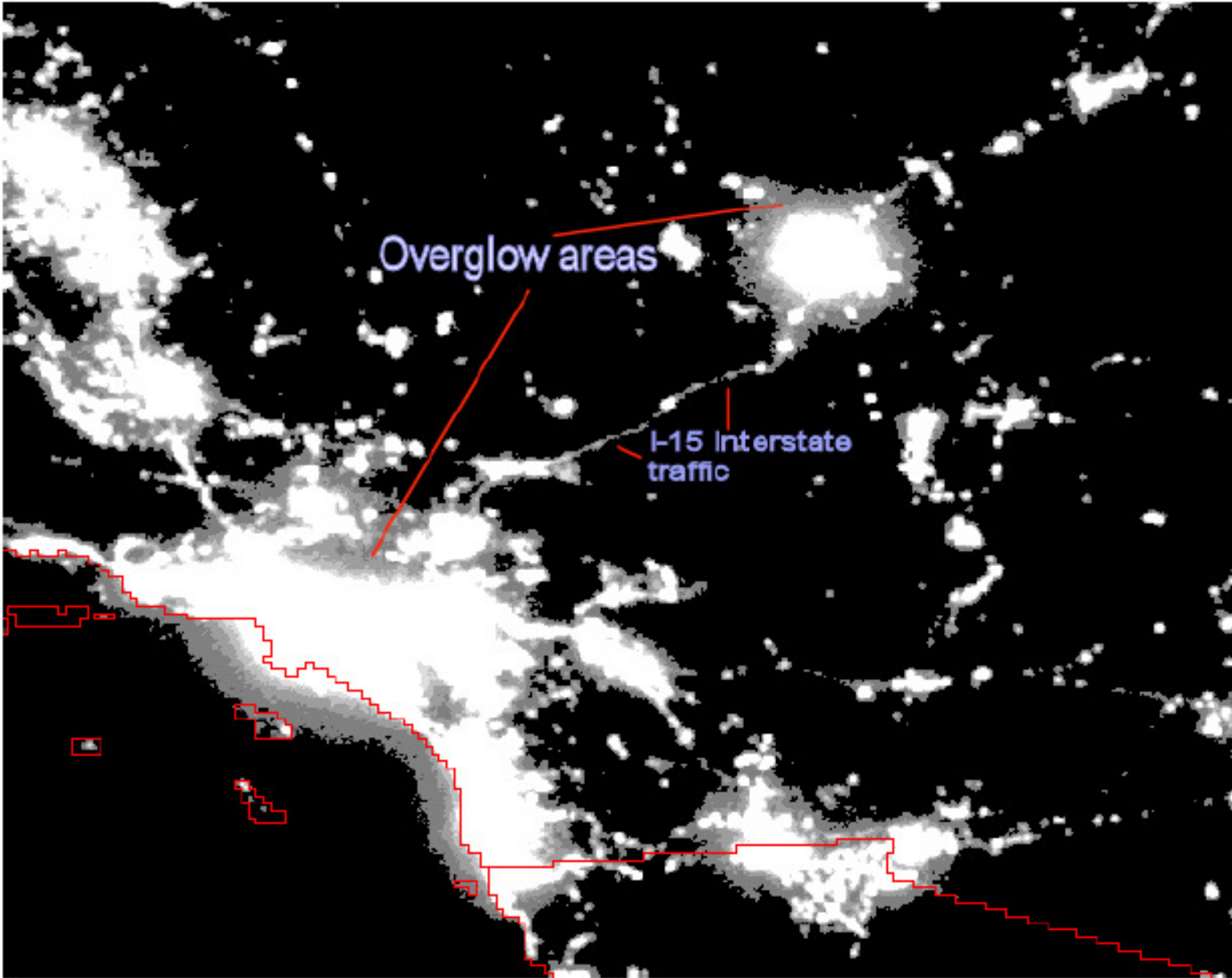
Errors of measurement of output

We grade countries A through E on data quality

    A: US

    C: China

    E: Somalia, Sudan

We then estimate the error of estimates for each country:

    - For both country level and grid cell level

    - For both time series and for density (output/area)

Sources:

    - Revision data and statistical discrepancy for national accounts

    - Revision data for grid cells

Main Results

1. For ***countries and cells***, the value added of luminosity is low for A and B countries; rises with lower grade; and is high for E countries. Luminosity has roughly equal value added for countries and cells conditional on grade.

2. Luminosity has value added for all countries and cells for ***output density.***

3. For ***low density*** countries, luminosity has a higher value added for cells; but the luminosity weight on low-density cells is smaller (puzzle!).

4. The major improvements in output measures must come from standard approaches because luminosity is (currently) too noisy.

Backup Slides

Productivity Program Researchers Source of Ph.D. Degree

Ph.D. Granting University (Multiple Ph.D. Graduates)

- Harvard (12)
- MIT (7)
- Stanford (7)
- Yale (7)
- UC-Berkeley (7)
- Chicago (4)
- Wisconsin (3)

Ph.D. Granting University (Each with one Ph.D. Graduate)

- Boston College
- British Columbia
- Ecole Nationale de la Statistique
- K. U. of Leuven
- Maryland
- Michigan
- Minnesota
- Northwestern
- Pennsylvania
- Penn State
- Texas - Austin
- University College – London

Current Primary Academic Affiliation of Productivity Program Researchers

Multiple RAs/FRFs at:

- UC – Berkeley (5)
- MIT (5)
- Northwestern (4)
- NYU (4)
- Boston University (3)
- Duke (3)
- Harvard (3)
- Chicago (2)
- Maryland (2)
- Minnesota (2)
- Penn State (2)
- Stanford (2)
- Toronto (2)
- UC – Los Angeles (2)

One RA/FRF at each of:

- Air Force Academy
- Arizona
- Brandeis
- British Columbia
- Case Western
- Clark
- Colorado
- Columbia
- K.U. of Leuven
- Maastricht
- Princeton
- Rensselaer Polytech
- Southern Maine
- Syracuse
- Tel Aviv
- Tokyo
- Toulouse
- UC - Davis
- UC- San Diego

Proportion of NBER Productivity Working Papers Authored by Non-Productivity Program Affiliates Has Been Increasing

Proportion of NBER Productivity Program Working Papers Authored by Researchers without a Primary or Secondary Appointment in the Productivity Program:

1985	1/11	9.1%
1990	3/14	21.4%
1995	4/28	14.3%
2000	11/56	19.6%
2005	29/72	40.3%
2009	21/74	28.4%
2010	19/60	31.7% (thru September 1, 2010)

NBER Productivity Program Researchers' Demographics

- Among 45 RAs, eight are age 65 or older, 24 are between 50 and 64 years old, and 13 are between 35 and 50 years old; none are < 35

- Eight of 45 (18%) RAs are female, 37 (82%) are male

- Among 14 FRFs, nine are 35 years old or older, and five are less than 35 years old

- Four of 14 (29%) FRFs are female, 10 (71%) are male

Forthcoming Events

- November 12-13, 2010: NBER/CRIW on *Wealth, Financial Intermediation and the Real Economy* (Charles Hulten, Michael Palumbo and Marshall Reinsdorf, Co-Organizers), Federal Reserve Board, Washington DC

- December 10, 2010: NBER Productivity Program Fall Meeting, joint in morning with the Organizational Economics group; afternoon Productivity Program only meeting co-organized by Ernst R. Berndt and Iain M. Cockburn

Interpreting these results

- Role of IP in realizing the full potential of genetic medicine
  - "Holy grain" of biology has not fulfilled grand expectations
  - Results suggest institutions mattered, beyond scientific factors

- Results also shed some light on the more general question of how IP affects subsequent innovation
  - One input into broader questions about design of IP systems
  - *Not* evaluating overall welfare effects of IP in this paper

Selection into Celera's IP

- Assess presence and magnitude of selection by comparing gene‑level observables across Celera, non‑Celera genes
  - Does selection appear consistent with historical accounts?

- Collect characteristics observable at the time of sequencing that were potentially correlated with commercial potential
  - Scientific papers published *prior* to a gene being sequenced
    - *E.g.* Studies suggesting Huntington's disease had a genetic basis
  - *Ex ante* known approximate location on the genome
    - *E.g.* Chromosome 19 hypothesized to be especially valuable

Selection into Celera's IP (2)
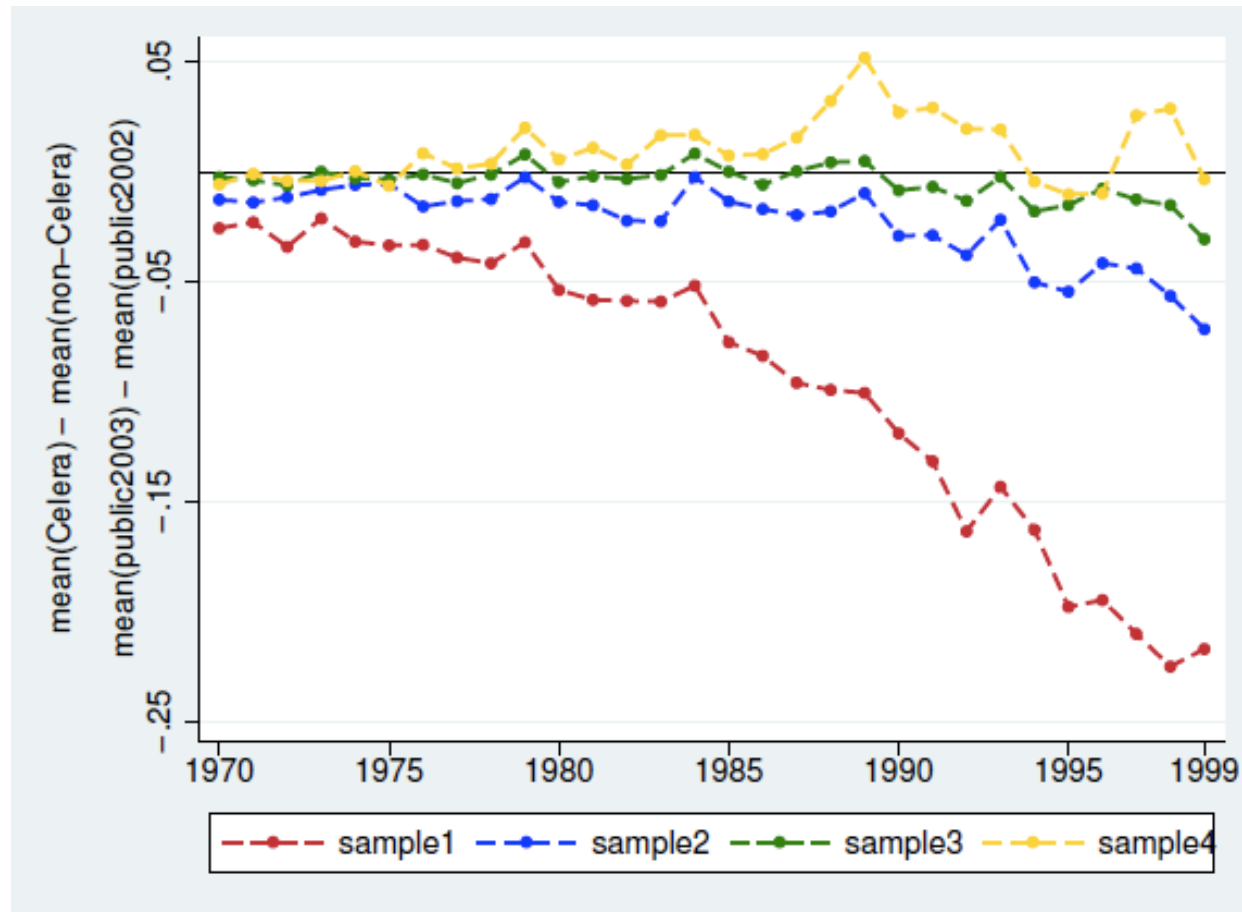
Sample 1: full sample; *Sample 2*: 2001 sample;
Sample 3: 2000 forward sample; *Sample 4*: Celera sample

Biotechnology Industry Is A Young Industry

U.S. Biotechnology Industry Timeline

1972
Cetus Founded

1976
Genentech Founded

1981
Genzyme Founded

1992
Amgen First Fortune 500 Biotech

2002
Human Genome Sequenced

1970

2009

1972
Stanford First Recombinant DNA

1982
First Recombinant Product-Insulin

2008
Economic Crisis & Retrenchment
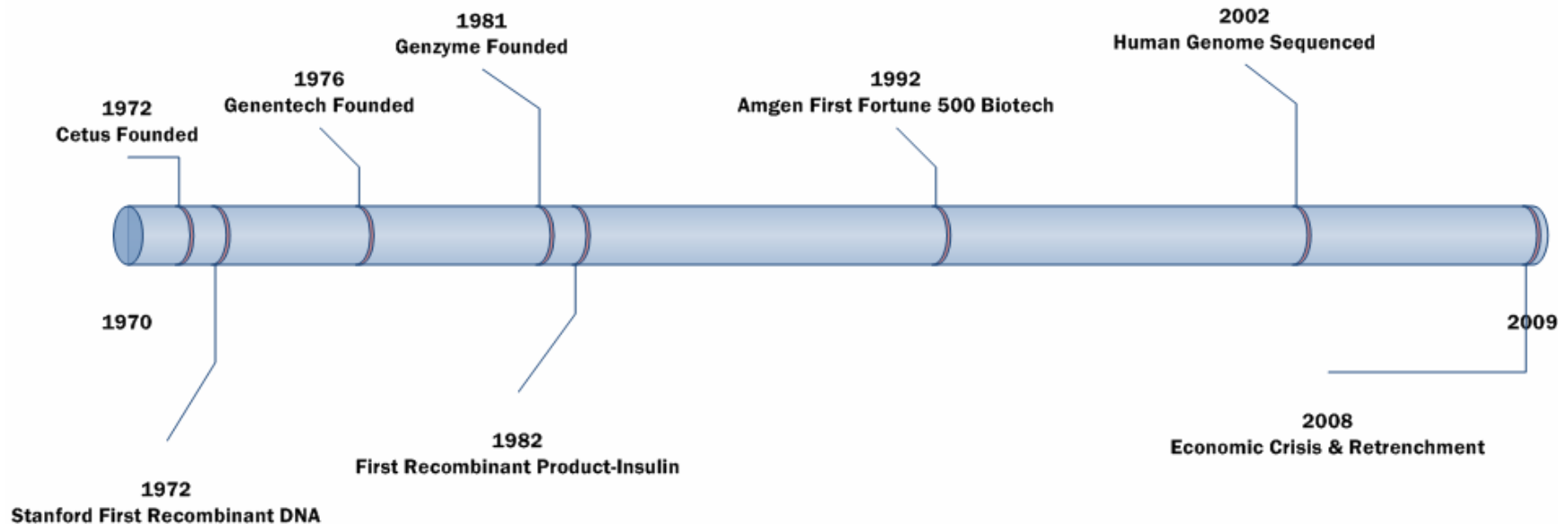
The Overlapping, but Distinct Paths of Small Molecule and Biologic Therapeutics

- Overall path and stages are similar
- Many individual steps quite different in practice
  - Active ingredient discovery and optimization
  - Manufacturing process
  - Regulatory review
  - End of legal exclusivity and new competitor entrant process

Simplified Small Molecule Life Cycle

Basic Research	Target Discovery	Hit Discovery	Medicinal Chemistry	PreClinical	Mfg Synthesis	Clinical Trials	NDA Review	Commercial	Exclusivity Expiry/ Generic Entry

	Similar Steps
	Differential Steps

?
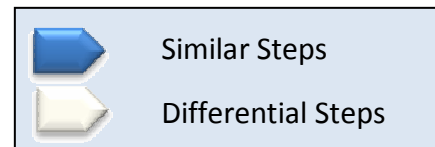
Simplified Biologic Life Cycle

Basic Research	Target Discovery	Recombinant Protein	Protein Optimization	PreClinical	Mfg Fermentation	Clinical Trials	BLA Review	Commercial	BioSimilar?

Creating the TABITHA Data Set

(TAB Innovative Therapeutics Historical Archive)

Core Data Set: IMS MIDAS$^{©}$ database of products, revenue and volumes

Annotation:

- Biologic Status
- WHO Therapeutic Area
- BEA GDP Deflator
- FDA Experience

Curation (QC, Filter, Transform):

- Novel therapeutic in date range
- Inflation adjustment & launch date alignment
- Annotation linkage
- Missing data screening
- Derived data
- Minimal threshold, idiosyncratic distribution and seasonal volatility filters
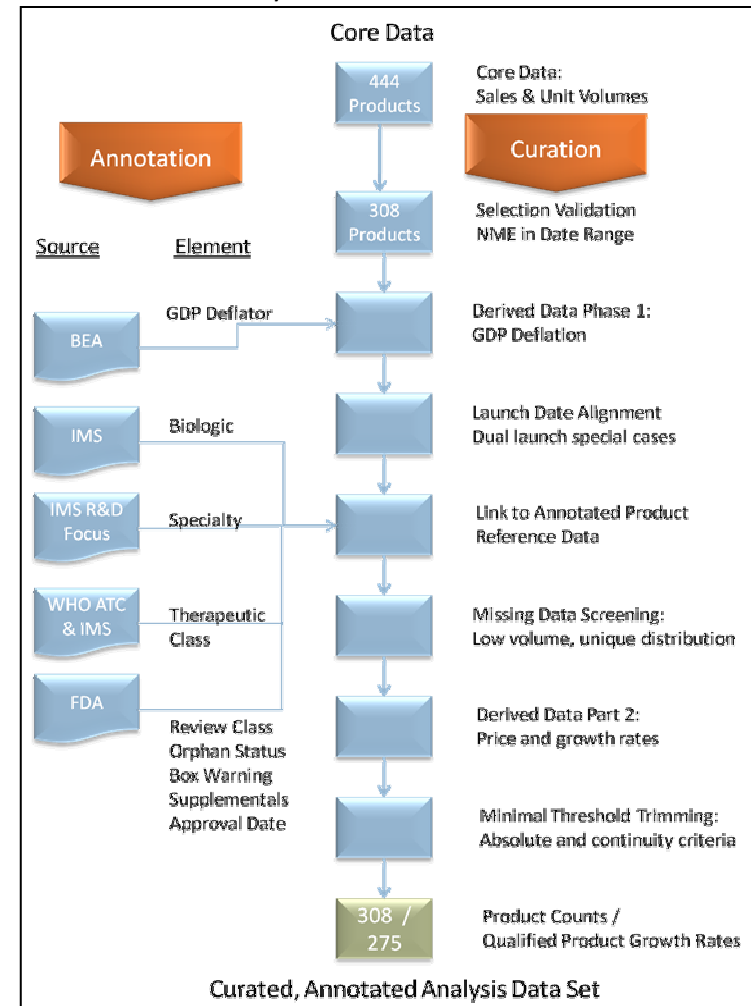
Biologic Proportion of Product Launches Stable Over the Period

- Decline in new product launches well known
- Biologic proportion stable across early and late sub-periods

Mean Number of Newly Launched New Molecular Entities, Small Molecules and Biologics, 1998-2003, 2004-2008							
		Mean			Percentage		
		98-03	04-08		98-03	04-08	Total
Biologic		10.3	6.8		31%	32%	31%
Small Molecule		23.3	14.4		69%	68%	69%
Total		33.7	21.2				

Similarities In Overall Mean Delays Masks Large Differences Among Therapeutic Classes

- No clear pattern of biologic or small molecule advantage
- Small numbers of products and large standard deviations in therapeutic classes
- Factors contributing to disparities not known

Days Delay Between FDA Approval and First Observed Sales by ATC Class, Biologics and Small Molecules									
	Biologic			Small Molecule			Total		
ATC1	Mean	Std. Dev.	Count	Mean	Std. Dev.	Count	Mean	Std. Dev.	Count
A: Alimentary Tract and Metabolism	128.3	196.0	16.0	63.3	152.7	26.0	88.0	171.2	42.0
B: Blood and blood forming organs	60.7	95.9	15.0	166.0	301.8	6.0	90.8	177.7	21.0
C: Cardiovascular System	-9.0		1.0	95.8	164.6	20.0	90.8	162.1	21.0
D: Dermatologicals	7.7	7.4	3.0	110.6	101.6	5.0	72.0	93.6	8.0
G: Genito-Urinary Systems and Sex Hormones				52.1	99.5	13.0	52.1	99.5	13.0
H: Systemic Hormonal Preparations, Excl. Sex Hormones And Insulins	117.7	79.3	6.0				117.7	79.3	6.0
J: Anti-Infectives For Systemic Use	42.4	50.5	23.0	27.5	86.5	38.0	33.1	74.8	61.0
K: Intravenous Solutions				154.0		1.0	154.0		1.0
L: Antineoplastic And Immunomodulating Agents	17.7	22.9	20.0	9.3	31.9	28.0	12.8	28.5	48.0
M: Musculo-Skeletal System	28.5	37.3	4.0	124.2	261.3	6.0	85.9	202.0	10.0
N: Nervous System	155.0		1.0	56.1	79.2	36.0	58.8	79.8	37.0
P: Antiparasitic Products				99.0		1.0	99.0		1.0
R: Respiratory System	11.0		1.0	142.3	179.2	11.0	131.3	175.0	12.0
S: Sensory Organs	8.0	9.9	2.0	34.5	86.4	10.0	30.1	78.9	12.0
V: Various	154.0		1.0	162.3	179.2	11.0	161.6	170.9	12.0
Grand Total	58.7	103.6	93.0	65.1	133.0	212.0	63.2	124.6	305.0

Specialists Important for Both Small Molecules and Biologics

- 68% of biologics prescribed predominantly by specialists
- PCPs primary prescribers of 53% of small molecules

Specialist and Primary Care Predominant Prescriber						
	Biologic		Small Molecule		Grand Total	
	Count	Percentage	Count	Percentage	Count	Percentage
Primary Care Driven ATCs	31	32%	112	53%	143	46%
Specialist Driven ATCs	65	68%	100	47%	165	54%
Grand Total	96		212		308	

Price Change Market Dynamics of Biologics and Small Molecules

**Mean Real Sales Growth (Quarter over Prior Year's Same Quarter)
from First Quarter of Observed Revenues,
All ATC Classes, Biologics and Small Molecules**

Higher growth of small molecules

Negative growth of small molecules

Mean Biologics

Mean Small Mol

	Qtr 6	Qtr 7	Qtr 8	Qtr 9	Qtr 10	Qtr 11	Qtr 12	Qtr 13	Qtr 14	Qtr 15	Qtr 16	Qtr 17	Qtr 18	Qtr 19	Qtr 20	Qtr 21	Qtr 22	Qtr 23	Qtr 24	Qtr 25	Qtr 26	Qtr 27	Qtr 28	Qtr 29	Qtr 30	Qtr 31	Qtr 32
Mean Biologics	128%	74%	63%	58%	56%	31%	31%	24%	20%	27%	22%	25%	14%	7%	23%	6%	5%	6%	5%	8%	1%	1%	4%	1%	3%	4%	1%
Mean Small Mol	170%	103%	81%	70%	64%	46%	38%	28%	25%	27%	23%	19%	20%	11%	10%	10%	6%	4%	3%	2%	3%	3%	4%	-1%	-3%	-3%	-4%
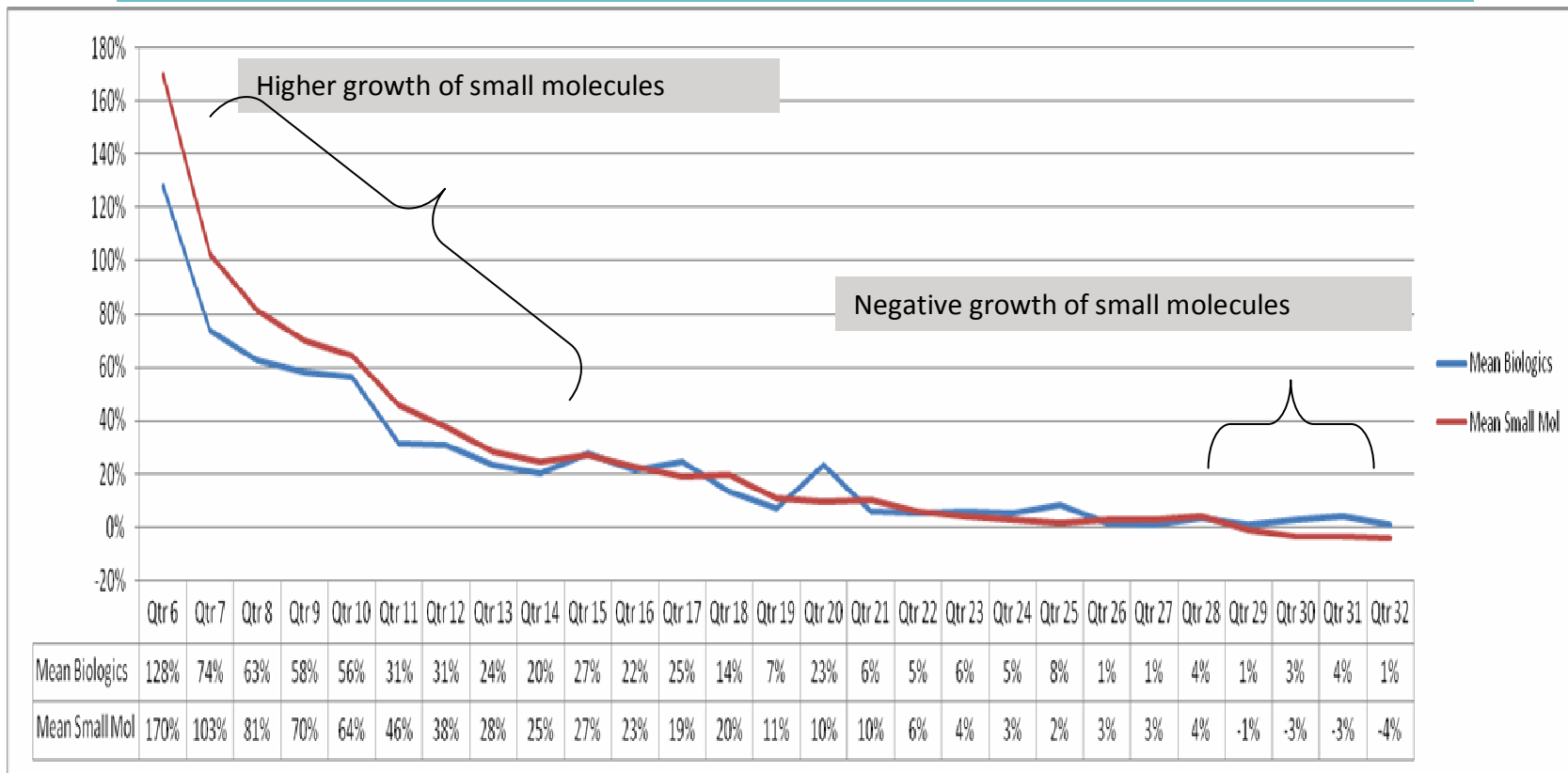
Biologics are a Large Portion of the Biopharmaceutical Pipeline

- If historic relative success rates continue, biologics may represent 50% or more of future US product launches

Biologics Percentage of Global Therapeutic Pipeline
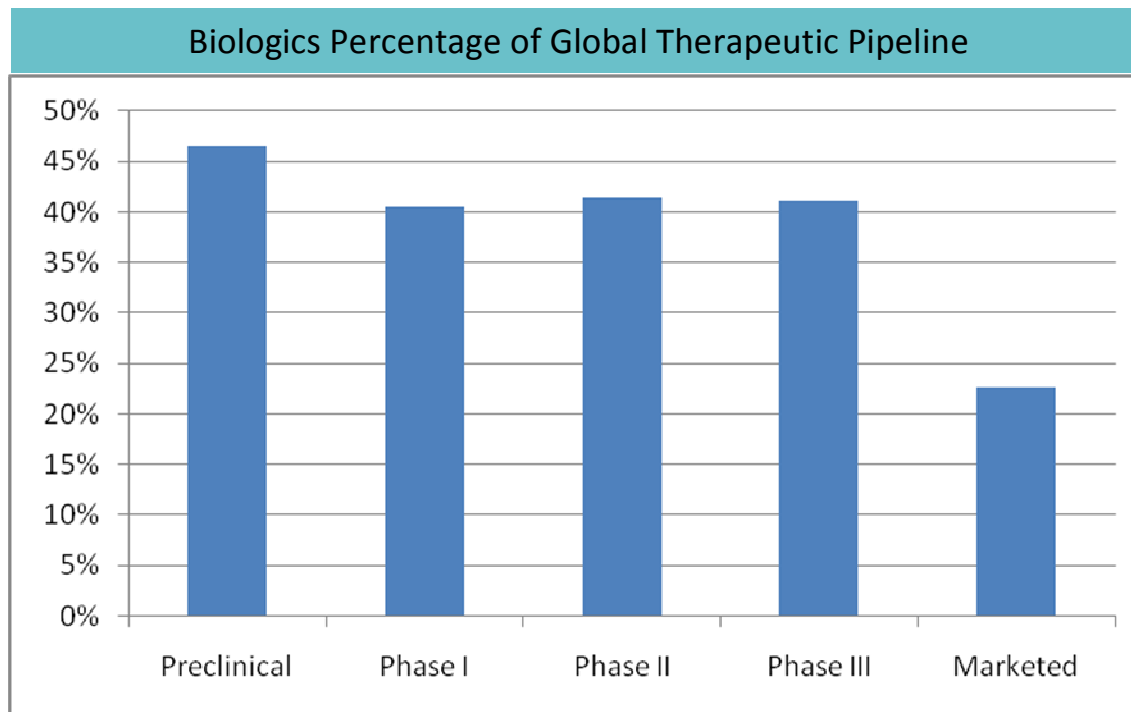
The analytical background

- Ultimate goal – test whether luminosity contains information for constructing true GDP, esp. for countries and cells with poor-quality data
- Major assumptions:
  - "True"output subject to measurement error *(y* = ln true output)*:

$$(1) \qquad y_i = y_i^* + \varepsilon_i$$

  - Luminosity with measurement error *(m* = ln true lum)*

$$(2) \qquad m_i = m_i^* + \xi_i$$

  - Structural relationship between luminosity and output

$$(3) \qquad m_i = \alpha + \beta y_i^* + u_i$$

* We are indebted to the study by Henderson, Storeygard, and Weil(2009) for suggesting a modification of our original modeling.

The analytical background (cont'd)

- Then we construct:
  - A luminosity-output proxy with adjusted β

$$(4) \qquad \tilde{\beta} = \left(\frac{\sigma_{y^*}^2 + \sigma_{\varepsilon}^2}{\sigma_{y^*}^2} \right) \hat{\beta}$$

$$(5) \qquad z_i = (1/\tilde{\beta}) m_i$$

  - An optimal synthetic measure of output by taking the optimal weights of conventional measures and our proxy

$$(6) \qquad x_i = \theta y_i + (1-\theta) z_i$$

  - Our central question: what are optimal weights on conventional and luminosity-proxy measures

The analytical background (cont'd)

- The error variance of X can be expressed as a function of θ

$$V(\theta) = E[\theta y + (1-\theta)z - y^*]^2$$

- Maximizing with respect to θ

$$(8) \quad \theta^k = \frac{\sigma_u^2}{\beta^2 \left(\sigma_\varepsilon^k\right)^2 + \sigma_u^2}$$

- Calculating parameters

  - σ_u^2 is mean square residual in the structural regression
  - β is error-corrected coefficient in the structural regression
  - σ_ε^2 is a prior error estimates for GDP for different country grades
  - k = country statistical grade (A,…,E)