

FAILURE



WHY SCIENCE IS SO SUCCESSFUL



STUART FIRESTEIN

Failure

Failure

Why Science Is So Successful

Stuart Firestein

OXFORD
UNIVERSITY PRESS

OXFORD
UNIVERSITY PRESS

Oxford University Press is a department of the University of Oxford. It furthers the University's objective of excellence in research, scholarship, and education by publishing worldwide.

Oxford New York

Auckland Cape Town Dar es Salaam Hong Kong Karachi
Kuala Lumpur Madrid Melbourne Mexico City Nairobi
New Delhi Shanghai Taipei Toronto

With offices in

Argentina Austria Brazil Chile Czech Republic France Greece
Guatemala Hungary Italy Japan Poland Portugal Singapore
South Korea Switzerland Thailand Turkey Ukraine Vietnam

Oxford is a registered trademark of Oxford University Press
in the UK and certain other countries.

Published in the United States of America by
Oxford University Press
198 Madison Avenue, New York, NY 10016

© Stuart Firestein 2016

All rights reserved. No part of this publication may be reproduced, stored in a retrieval system, or transmitted, in any form or by any means, without the prior permission in writing of Oxford University Press, or as expressly permitted by law, by license, or under terms agreed with the appropriate reproduction rights organization. Inquiries concerning reproduction outside the scope of the above should be sent to the Rights Department, Oxford University Press, at the address above.

You must not circulate this work in any other form
and you must impose this same condition on any acquirer.

Library of Congress Cataloging-in-Publication Data
Firestein, Stuart.

Failure: Why Science Is So Successful / Stuart Firestein.
pages cm

Includes bibliographical references and index.

ISBN 978-0-19-939010-6

1. Failure (Psychology). 2. Science—Philosophy. 3. Discoveries in science.
I. Title.

BF575.F14F567 2015

501—dc23

2015009156

1 3 5 7 9 8 6 4 2

Printed in the United States of America
on acid-free paper

Contents

<i>Acknowledgments</i>	vii
Introduction	1
ONE	
Failing to Define Failure	7
TWO	
Fail Better: Advice from Samuel Beckett	25
THREE	
The Scientific Basis of Failure	39
FOUR	
The Unreasonable Success of Failure	49
FIVE	
The Integrity of Failure	63
SIX	
Teaching Failure	71
SEVEN	
The Arc of Failure	97
EIGHT	
The Scientific Method of Failure	119
NINE	
Failure in the Clinic	135

vi *Contents*

TEN

Negative Results: How to Love Your Data When It's Wrong 145

ELEVEN

Philosopher of Failure 167

TWELVE

Funding Failure 177

THIRTEEN

Pharma Failure 205

FOURTEEN

A Plurality of Failures 215

FIFTEEN

Coda 247

Notes and Works Consulted 253

Index 275

Acknowledgments

So many people deserve to be acknowledged for their many contributions that I am terrified of failing to be inclusive. Among the most important, though, is Alex Chesler. Right from the beginning Alex has been involved, as a teaching assistant for my first course in Ignorance while a graduate student in my laboratory and continuing with conversations over the years about failure and ignorance and the role they play in science. Alex could easily have coauthored this book with me, and we discussed precisely that on numerous occasions. However, the rigors and responsibilities of starting a new laboratory (at NIH) and a new family (two children with wife Claire, who was also a graduate student in my

laboratory) made it impractical. But his mind and imprint are all over this book.

I was incredibly fortunate to have the opportunity to spend a sabbatical year (10 months in all) as a Visiting Scholar in the Department of the History and Philosophy of Science at Cambridge University. This book would have been finished a year earlier if it had not been for that sabbatical. And it would have been much the worse for it. The colleagues I interacted with there, the lectures that I attended, the long conversations over beer in the pubs (yes, it really is like that) added so much to this book that I can't imagine how I thought I could have written it before going there. A year's sabbatical does not make one a philosopher or historian, but it does develop an appreciation for those pursuits and a sense of the value that they bring to understanding science and how we do it, and even why we do it.

Although the entire Department welcomed me in the most inclusive way, I have to single out Hasok Chang, who seems to have inherited the unenviable job of being my liaison in the Department. Generous is not nearly sufficient to describe his treatment of me. Not only with his time, but more importantly with his ideas and perspectives, and questions and critiques. You will see that I reference him several times in this book. He is one of the most important thinkers, and writers, and doers in science today—by which I mean the entire effort, from teaching to experimenting to contextualizing to

chronicling and documenting it. I am thrilled that he and his brilliant and equally generous wife Gretchen continue to count me as a friend and colleague.

Many others at Cambridge listened to me rant about failure and responded with thoughtful and challenging ideas. Many read portions of the book here and there and commented freely. I have stolen mercilessly from them. I can hope only that they see it as the flattery which it is. I am also happy to be able to say that I was welcomed as an honorary Fellow at Kings College. There I shared meals and wine and conversation with people who have perfected the epicurean art of blending sociality with intellect. The opportunity to have dinner or lunch on any given day with scholars of music, Russian literature, mathematics, classics, biology, or psychology was for me like being the proverbial kid in a candy store. I cannot thank the Fellows at Kings College enough for so many of the memories of the most memorable year of my life.

The Alfred P. Sloan Foundation and the Solomon R. Guggenheim Foundation provided funds to support my time in Cambridge and for many of the other expenses associated with producing the manuscript. I am deeply indebted (not literally, fortunately) to them for their show of faith and their interest in the subject. I hope that they are proud of what has come from their investment.

As with *Ignorance* before it, I find it a bit ironic to thank people for their contributions to *Failure*. Believe me, though,

they are responsible for whatever is successful here. Many colleagues read over versions of the manuscript from the early stages to late in its development. Among them I especially include Anne Sophie Barwich, a newly minted PhD who can be intensely critical and immensely fun at the same time, Charles Greer, Matthias Girel, Peter Mombaerts, Jonathan Weiner, and Matt Rogers, and Brian Earp, a student and now good friend I met while at Cambridge.

I am also quite fortunate in being a member of a writing group, called Neuwrite, composed of scientists, from graduate students to lab heads, and writers, from students to professionals, all of whom are interested in the unique problems of writing good science for a wide audience. Remarkably, this group has continued to meet regularly for over seven years, and from it have emerged books, magazine articles, essays, newspaper pieces, films, and short stories that have appeared in a wide variety of venues, both online and in print (see <http://www.columbia.edu/cu/neuwrite/members.html>). Several chapters of this book have been workshopped by this group, and I have gotten many useful and challenging comments from the group and many of its members individually.

I am very lucky to have the backing of Oxford University Press, in particular Joan Bossert, who has been a great supporter, exceptional editor, and very good friend and martini partner; and the excellent staff of publicists, editors, and production people who worked on *Ignorance* and now on *Failure*

and must be wondering what in the world could be coming next.

I was incredibly fortunate to have leased a small house from the Duncans, former Cambridge faculty members, on the aptly named Eden St. This house provided the perfect setting for reading, thinking, and, most importantly, writing. I tended to a growing community of diverse birds who visited regularly in the backyard. It still makes me a little homesick not being there.

Finally, I must acknowledge, even though that word hardly captures the debt I owe them, my wife and daughter, who went through *Ignorance* with me and then followed right along through *Failure*. They read this manuscript many times, kept me from straying more often than you could imagine, and contributed many important ideas. Their unfailing faith and support in one mad project after another is of course well beyond priceless. Assuming they are not completely crazy, they are the very best two people in the world.

Failure

Introduction

Perhaps the history of errors of mankind, all things considered, is more valuable and interesting than that of their discoveries. Truth is uniform and narrow . . . but error is endlessly diversified.

—Benjamin Franklin

This book has failure written all over it.

Literally of course, but metaphorically as well. So failure will stalk this book, and it may occasionally win a round. But if I get it right, you'll understand that those failures are an important part of the book, an absolutely necessary ingredient. A book on failure cannot just be a lecture; it must be a sort of demonstration as well. And so now, by some sleight of hand, I have at least partly inoculated myself against failing by telling you that the theme of the book is how important failures are. Come to think of it, that's also a theme—that we must make and defend a space for noncatastrophic failure, a place where failure can happen regularly.

2 Failure

This book follows, and is kind of an extension, of another book I wrote recently called *Ignorance: How It Drives Science*. As you can see I'm carving out a nice, neat, little niche for myself. It might seem like I am becoming a merchant of despair. In fact I find both of these subjects to be uplifting. Although ignorance and failure are commonly thought of in a negative light, in science they are just the opposite: they are where all the interesting action is. This will be a key point in this book—that failure in science is fundamentally different from all the other failures you've read about in self-help and business books and articles in *Wired* and *Slate*. It is a kind of failure we don't appreciate enough. Not understanding this, not appreciating failure sufficiently, leads to distorted views of science and denies one a surprisingly useful but rarely considered version of failure. I hope that on this one point I don't fail you.

Science, the great intellectual achievement of modern Western culture, is often depicted as resting on pillars of great foundational strength and intellectual might.

These pillars are variously identified as KNOWLEDGE and REASON, or FACT and TRUTH, or EXPERIMENT and OBJECTIVITY. Quite impressive. Students are regularly asked to approach science in the reverential way that these ponderous pillars demand. Perhaps such pillars are the correct depiction for textbook science—the stuff that is frozen in time and that generations of these same poor students

have been required to master, by which we usually mean *temporarily memorize*. But then there is current science, the real stuff that goes on every day in laboratories and in minds across the world. Science rests, I am afraid to say, on two somewhat less imposing sounding pillars—IGNORANCE and FAILURE.

Yes, that's it, the whole tremendous edifice. The costly research programs, the years of education, the dedication of cadres of PhDs, teetering on top of Ignorance and Failure. But without these two, the entire business would come to a standstill. In fact, Ignorance and Failure are not so much pillars as engines that propel science forward. They make it at once a reckless endeavor and a conservative process, a creative enterprise composed of mind numbing reams of data. I understand that this view of science, beholden to Ignorance and Failure, is probably not the common perception, and that few outside of practicing scientists will immediately recognize the truth of this proposition. But I bet that anyone who has made a career of science, reading this now, is nodding in agreement. Indeed, every scientist to whom I have mentioned that I am writing a book on failure has immediately offered to contribute a chapter! Remarkably, most of us make a pretty good living doing this kind of work and virtually every scientist I know loves their work. So how could that be, composed as it is mostly of ignorance and failure—with perhaps a dash of accident or serendipity thrown in?

It may seem that I'm putting you on here, pretending to reveal some dirty little secret just to grab your attention. But the thing is, it's not a secret at all: it's general knowledge, inside of science. Somehow outside of the scientific establishment it seems we do a very bad job of letting everyone else in on what we do. So many things just get taken for granted that it never occurs to us to make it explicit. You know more or less what lawyers do, what accountants do, what journalists do, what car mechanics do—even if you couldn't do any of those things yourself. But when I tell a crowd of my daughter's friend's parents that I'm a scientist, all they want to know is what I do. Actually *do*, during the day, every day.

One curious thing about this book was that it never coalesced into a linear argument with some internal logic driving it forward. I didn't start the chapters in any particular order, and I kept working on them in no particular order. They are more like essays than chapters, each a reflection on some aspect of failure and science. The famed immunologist and science writer Sir Peter Medawar wrote a piece for the *Saturday Review* titled "Is the Scientific Paper Fraudulent?" His claim was not that scientific papers were untrue, but that they were constructed in a way that did not reflect the actual experimental or intellectual processes at work. They were reconstructed in some narrative order intended to drive home the point but were not an accurate record of the way it actually happened. This book is sort of just the opposite. It

has not been put together in some carefully logical order that builds to a convincing and unassailable argument. It's more a collection of ideas, some of which I hope are new to you. They were to me.

One of the things I do hope this book will accomplish is to show science as less of an edifice built on great and imponderable pillars and more as a quite normal human activity. I don't mean by knocking it down a peg or two, but rather by building it up as a remarkable and surprisingly accessible way of seeing the world. Science is accessible to everyone because really, at its core, it is all about ignorance and failure, and perhaps the occasional lucky accident. We can all appreciate that.

ONE

Failing to Define Failure

A real failure does not need an excuse. It is an end in itself.

—Gertrude Stein

I have chosen this deceptively simple sounding statement, so typical of Gertrude Stein, to open this book because it gets so quickly to the heart of the matter. It challenges, right from the beginning, our idea of what a failure may be. What kind of a failure is Stein talking about here? What makes a “real” failure? Are there “unreal” failures, or lesser failures?

Like so many important words, *failure* is much too simple for the class of things it represents. Failure comes in many flavors, and strengths, and contexts, and values, and innumerable other variables. Nothing just stands alone as a failure without knowing something more about it. In the famous *Encyclopédie* of the French enlightenment, Diderot and d’Alembert (1751–1772) under the entry for *erreur*, which

seems intended to cover failure as well, caution that there is no way to develop a general description or classification because *erreur* comes in so many forms. I started this project with what I thought were a few clear ideas about failure and its value in the pursuit of scientific explanations. What surprised me was how quickly those few ideas generated dozens of questions.

There is a continuum of failure, not just one narrow kind. Yes, there are failures that are just mistakes or errors, and they may often be no more than an unfortunate waste of time. There are failures from which you learn simple lessons: be more careful, take more time, check your answers. There are failures that can be taken as much larger life lessons: a failed marriage, a failed business venture; painful but perhaps character building. There are failures that lead to unexpected and otherwise unavailable discoveries: they often seem like serendipity, an accidental failure that opened a door you didn't even know was there. There are failures that are informative: it doesn't work this way; there must be some other way. There are failures that lead to other failures that eventually lead to some kind of success about learning why the other paths were failures. There are failures that are good for a while and then not—in science you might think of alchemy, a failure that nonetheless provided the foundations of modern chemistry.

Failures can be minimal and easily dismissed; they can be catastrophic and harmful. There are failures that should be encouraged and others that should be discouraged.

The list could go on. But I don't want to get sidetracked into a lengthy polemic trying to define failure, which would surely fail. We'll come upon all sorts of failures as we proceed, and we would do best to think of them as discoveries, not contradictions. Rather, I want to focus on the *role* that failure, in all its many identities, plays in science and how it contributes to making it such a successful enterprise.

Stein seems to be complaining about the common response to a failure—which is apology. Failure as mistake, unintended or unavoidable or because of some shortcoming that you are responsible for. Failure as the result of stupidity and naiveté that requires excuses and apologies. Why did you let that fail? Can't you do any better than that? Or, perhaps less antagonistic but no less disappointing, failure as inevitable. Well, that wasn't likely going to work. What did you expect? What a stupid thing to have even tried. And so forth. Stein, in that first simple sentence, identifies all these bad failures, useless failure, failures that demean failure.

Instead, how about failure that stems not from ineptitude, inattention, or incapacity. (True, even those occasionally turn out to reveal something unexpected and sometimes wonderful. But I wouldn't depend on them. Sloppy indifference can get you only so far.) A real failure is different from all those

that need or are accompanied by an excuse—because it needs no excuse.

So what are good failures? Ones that need no excuse and are an end in themselves? Not really an end in the typical sense—that is, not an end where you give up trying anything else. Rather an *end* in the sense of something new and valuable. Something to be proud of and therefore requiring no excuse, even if it was “wrong.”

Are there really such failures? Of course there are the mistakes we learn from, the errors that can be corrected, the failures that can be turned to success. But I’d like to take a chance here and venture that Stein meant something deeper than that. That she really meant meaningful failure. In the limit, this could mean that you might produce nothing but meaningful failures for your entire life and still be counted a success. Or at least never need to apologize. Is that really possible? What are these magical failures?

I have two possible answers. The first is that failures that are ends in themselves are interesting. Interesting is another word that one has to be careful about. It’s easy to use, but then it’s kind of vague and subjective. Is there anything that’s interesting to everybody? I doubt that. But if we take interesting as a descriptor rather than an identifier—that is, a quality of something and not necessarily a particular thing itself—then we can perhaps come to an understanding. When the same Gertrude Stein was asked to write a piece

about the atom bomb (shortly after its use in WW2 and, as it turns out, shortly before her death in 1946), she responded that it held no interest for her. She liked detective stories and that sort of literature, but death rays and super weapons were not that interesting because they left nothing behind. Someone sets off a bomb or some weapon of mass destruction that kills everybody and ends everything. So what's to be interested in? Certainly better if it didn't happen, but if nothing is all you're left with, then who cares? So maybe it's what's left that could make something an interesting failure. Good failures, we could call them Stein Failures, are those that leave a wake of interesting stuff behind: ideas, questions, paradoxes, enigmas, contradictions—you know what I mean. So that's one kind of successful failure I'm pretty sure about.

Here's the second idea. Is it the actual failure that is the end in itself? Or is it the willingness to fail, the expectation of failure, the acceptance of failure, the desirability of failure? Can you imagine making failure desirable? Can you imagine aiming at failure? Can you appreciate making failure your goal?

You *can* if you have the right idea about the word failure—what I hope to convince you is the scientific version of failure. It is more than a stupid error, more than a shortcoming on your part, more than a miscalculation, more even than a chance to improve. Yes, more even than failures as life lessons. I know we all believe that a failure can be valuable

if you learn something from it. After all, that's what we call experience. But how about a failure that does not aim at later self-improvement? How about failures that really are *an end in themselves*?

In this sense virtually all of science is a failure that is an end in itself. This is because scientific discoveries and facts are provisional. Science is constantly being revised. It may be successful for a time; it may remain successful even after it has been shown to be wrong in some essential way. That may seem strange, but good science is rarely completely wrong, just as it is never really completely right. The process is iterative. We scientists hop from failure to failure, happy with the interim results because they work so well and often are pretty close to the real thing.

Newton was famously wrong about two little things—time and space. They are not absolute. Gravity is not explained by the attraction between the centers of massive bodies, although it looks that way and can be usefully described that way. To the extent that we can explain it at all, it seems to be best understood, for now, as an emergent phenomenon of mass creating curvature in space. An imperfect but useful analogy is the way a heavy bowling ball on a mattress causes a depression and things placed on the mattress tend to fall toward it, as if they were being attracted to it. But Newton's failure in that one regard, even though it seems like a fundamental part of the theory of gravity, is not at all fatal to the success

of his work. His equations quite accurately describe action at a distance between two bodies—sufficiently well to calculate how to dock a rocket with a space station orbiting some 250 miles away and moving at a speed of 17,000 miles per hour.

Nonetheless, there was a nagging inconsistency in Newton's model over what appeared as two different kinds of gravity. This inconsistency was what needled Einstein so much that he was ready to take a most unintuitive, illogical perspective. Although it's not exactly how Einstein thought about it, these two kinds of gravity are most easily experienced as the loss of gravity—weightlessness. One of them can be felt as distance from a massive body (the weightlessness experienced in outer space), and the other is due to acceleration (the weightless feeling you would have in a rapidly dropping elevator). They seem to be from two different and unrelated causes—the mass of a nearby body and the force resisted by inertia, or acceleration. Two hundred and fifty years later Einstein essentially corrected the failure of that part of Newtonian mechanics by showing that in the correct inertial frame, one that does not assume absolute time or space, the two kinds of gravity are the same.

Granted, it turned out to be a rather major correction, requiring a Copernican-sized shift in our point of view. But as with Copernicus it didn't require throwing everything else out. We continue to live our everyday lives in a Newtonian world where space and time seem sufficiently absolute, just

as we continue to live most of our lives in a pre-Copernican world where the sun “rises” and “sets.” That oversimplifies the story a great deal (see Notes), but the point is that Newton was successfully wrong and it was the very failed part of his model that led to Einstein’s remarkable insights. Pretty good work.

A failure can be even less successful—that is, wholly incorrect—and still useful. An example from biology might be the longstanding principle known as “ontogeny recapitulates phylogeny.” This tongue twister of a phrase, coined in 1866 by the “father of embryology,” Ernst Haeckel, is simply a slightly bizarre attempt at making a complicated concept memorable by forming a jingle about it. It means that over the course of its development an embryo in the egg (or uterus) appears to go through all the stages of evolution of that organism. For example, mammals early in embryonic development have what appear to be gill-like structures, making them look a bit like fish. These structures eventually develop into our jaws and other muscle and bone groups of our heads and throats but have nothing directly to do with respiration, as gills do for fish. In fact, Haeckel’s concept is completely wrong, even though it held sway for decades and led to many advances in embryology. Not only is it wrong about embryology, it is wrong about evolution. We didn’t evolve from fishes (or apes for that matter); we shared a common ancestor that evolved into both of us, in the case of fish some 500 million

years ago, and in the case of apes only about 85 to 90 million years ago.

Nonetheless, this failed ontogeny-phylogeny concept gave rise to important ideas about how development proceeds in clearly established stages, and that structures do evolve from earlier forms, possessing a common ancestry even if a contemporary divergence. Haeckel's work was painstaking and actually started the branch of science we today call embryology. In particular, he introduced comparative anatomy and development—that is, the notion that we can learn a great deal by making comparisons across species. This showed crucially that not only were species related but that their development proceeded in a similar way along certain principles. The value of this “failure” to modern biology cannot be overestimated. On the other hand, it remains damaging in that there are many people who still believe in it because they were taught it as schoolchildren. You remember, the silly business about having had a tail when you were an embryo.

You could object that Newtown's and Haeckel's failures eventually led to successes and were not therefore really ends in themselves. I think that's too much to ask of failure. Failures like these not only lead to greater insights, they often lead to very unpredictable insights. They force us to look at a problem differently because of the particular way in which they failed. This could be considered the case with Einstein's recognition that Newton's little failure was actually a

fundamental misconception about time and space. We expect success to lead us to even greater success. What may not be so obvious is that failure can do the same.

These then are what I would call the failures that need no excuse, that stand shoulder to shoulder with success. They are the packing material, the innards, of science, and not giving them their full due is to miss more than half of what science is about and how it works. The big job I hope to do here is to remedy that.

. . .

There are many trivial things that can, and have, been said about failure. They are the kinds of aphorisms commonly found in Chinese restaurant fortune cookies. I'll sum them up in a paragraph and then we can get on to the interesting parts of it—the much wider and deeper functions of failure that are undeservedly ignored or, worse, thoughtlessly rejected as undesirable.

So then here we go: failing is part of succeeding. Failure builds character. Those who haven't failed haven't tried. You never know yourself until you've had a failure. You have to learn how to pick yourself up and get back in the game. And so on. I'm sure you can think of other, similar platitudes. And they're all okay advice, especially when you have someone on the phone who is really distraught over a recent failure in love or work or sport. Sure, failing is part of life and managing it is important for your happiness. And there are innumerable